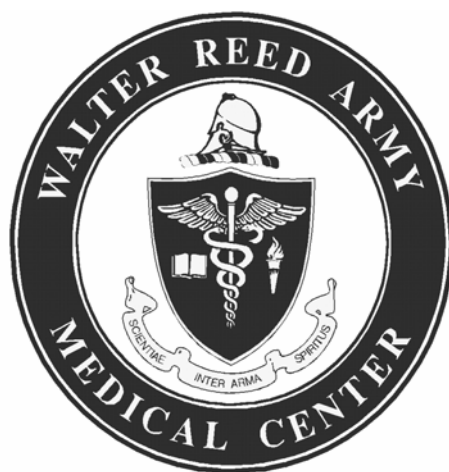


**DEPARTMENT OF CLINICAL INVESTIGATION (DCI)**

# **ANNUAL RESEARCH PROGRESS REPORT**



# **FISCAL YEAR 2003**

**WALTER REED ARMY MEDICAL CENTER, WASHINGTON, DC**

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13. ABSTRACT (Maximum 200 words) The Annual Progress Report documents all research protocols, both new and continuing, reviewed during FY 03 by the Clinical Investigation Committee (CIC) and the Human Use Committee/Institutional Review Board (HUC/IRB) of Walter Reed Army Medical Center (WRAMC). Continuing research review is administered by the Research Review Service (RRS), Department of Clinical Investigation (DCI), WRAMC. A detail summary sheet of each protocol giving the objective, technical approach, and progress is presented. Personnel rosters, DCI accomplishments, funding information, and known publications and presentations by the WRAMC professional staff are listed for FY 03.				
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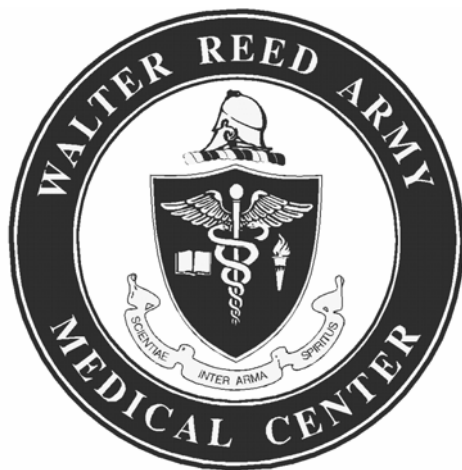
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**DEPARTMENT OF CLINICAL INVESTIGATION (DCI)**

# **ANNUAL RESEARCH PROGRESS REPORT**



## **FY 2003 VOLUME I**

**WALTER REED ARMY MEDICAL CENTER, WASHINGTON, DC**

The Department of Clinical Investigation continued to perform full services despite a major shortfall in staff personnel. Four civilians left DCI and have not been replaced to date. One contractor left WRAMC and was not replaced; the DCI Assistant Chief deployed to Iraq in February 2003, and the DCI NCOIC was on extended TDY attending ANOC School. Despite the increased amount of work for the remaining DCI staff, we processed protocols, held CIC and HUC meetings with minimum disruption, and accomplished the regulatory function entrusted to us. We were not able to plan for a research course for FY 03, but instead promoted a web-based course. This year, we started a short version of the research course to re-certify investigators who took the long course three years ago or longer. The education of investigators translated to an increase of research protocols over the years, an enhancement of quality in proposals and studies, and possibly a better protection of research subjects. We were able to continue the statistical course and the molecular biology course. Both were oversubscribed and received glowing evaluations. This year, refurbishment of the permanent housing of the DCI research laboratory was finished, and the laboratory was moved from temporary quarters (where it had been for the last three years) to Building 7. The renovation has afforded state-of-the-art laboratories to the WRAMC research program. We were able to hire a GS-13 immunologist for the research laboratory. He brought in-depth knowledge of immunological methods and expanded the capability of the laboratory. Extramural financing of research at WRAMC continued at a solid pace, probably as a result of the outstanding research that is conducted in this medical center. The Bailey K. Ashford competition brought in a record number of applicants and oral sessions. Poster sessions were set up to display the research performed by residents and fellows at WRAMC. It was highly successful, and the winners received medals, U. S. Army commendations, and a monetary prize. All in all, it was a successful year despite considerable decrease in manpower.

A. Objective

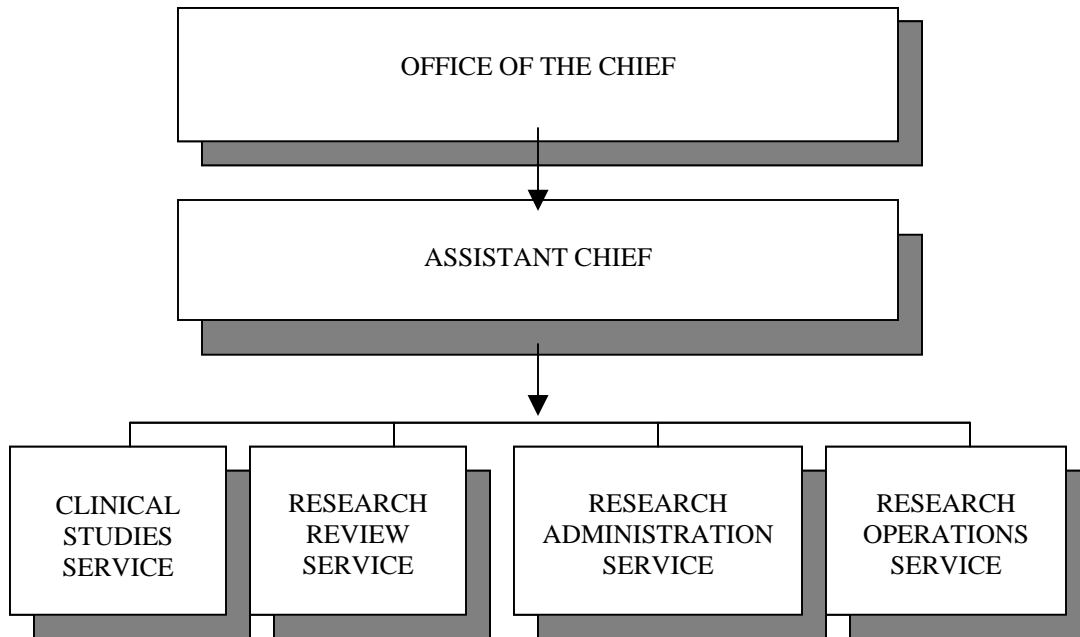
The Department of Clinical Investigation (DCI) of the Walter Reed Army Medical Center (WRAMC) is headed by COL Maria H. Sjogren, MC. The mission of the DCI is to implement and manage the Clinical Investigation program at WRAMC by promoting, supporting, coordinating, planning, conducting, and publishing ethical and scientific inquiry into clinical health problems of beneficiaries of the military health care system, to include studies in humans and animals. The motto of the Department of Clinical Investigation (DCI) is SHARPP: Striving to Help All Researchers from Planning to Publication.

B. Technical approach

The clinical investigation program at WRAMC is conducted in accordance with the following regulations:

AR 40-7	Use of Investigational Drugs in Humans and Use of Schedule I Controlled Drug Substances
AR 40-38	Clinical Investigation Program
AR 70-18	The Use of Animals in DOD Programs
AR 70-25	Use of Volunteers as Subjects of Research
TB MED 525	Control of Hazards to Health from Ionizing Radiation Used by the Army Medical Department
WRAMC 70-1	Clinical Investigation Program, WRAMC Research Activities
WRAMC PAM 40-112	Medical Services – Human Biological Specimen Banking
WRAMC 40-113	Medical Services – Health Information Privacy
45 CFR 46	Protection of Human Subjects
45 CFR 160, 164	Standards for Privacy of Individually Identifiable Health Information
21 CFR 50, 56	Food and Drug Administration
32 CFR 219	Protection of Human Subjects
DOD 3216.1	Use of Laboratory Animals in DOD Programs
DOD 3216.2	Protection of Human Subjects and Adherence to Ethical Standards in DOD Supported Research
DOD 6025.LL-R	DOD Health Information Privacy Regulation
DOD 6000.8	Funding and Administration of Clinical Investigation Programs
NIH Guidelines For Research Involving Recombinant DNA Molecules	

C. Organization scheme



D. Staffing

**OFFICE OF THE CHIEF**

Description	Grade	MOS	Branch	Name	Activity
Chief	O6	61F00	MC	Sjogren, MH	DCI
NCOIC	E6	91K40	NC	Thomas, L	DCI
Secretary	07	0318	GS	Lewis, L	DCI

**RESEARCH REVIEW SERVICE**

Description	Grade	MOS	Branch	Name	Activity
Chief	14	1530	GM	Chang, AS	DCI
IRB Admin	13	0601	GS	Bartlett, E	DCI
Statistician	12	1530	GS	Howard, RS	DCI
Statistician	12	1530	GS	Tuamokumo, F	DCI

Clinical Nurse Spec	12	0610	GS	Porter, MD	DCI
Clinical Nurse Spec	12	0610	GS	Kessler, DD	DCI
Tech Writer-Ed Med/Sci	11	1083	GS	Miskovsky, VJ	DCI
Clinical Studies Spec	09	0301	GS	Green, IL	DCI
Clinical Studies Tech	07	0303	GS	Rosen, D	DCI
Editorial Asst	07	1087	GS	Beltz, K	DCI
Editorial Asst	07	1087	GS	Vacant	DCI
Clinical Studies Spec				Stewart, C	HMJF
Med Lab NCO	E5	9K20	NC	Johnson, C	DCI

#### **RESEARCH ADMINISTRATION SERVICE**

<b>Description</b>	<b>Grade</b>	<b>MOS</b>	<b>Branch</b>	<b>Name</b>	<b>Activity</b>
Chief/Rsch Admin	12	0670	GS	Word, D	DCI
Computer Spec	12	2210	GS	Rose, JG	DCI
Computer Spec				Durant, G	Contract
Rsch Protocol Coord	12	0610	GS	Vacant	
DCI Grant Manager	11	1101	GS	Brunson, R	DCI
Administrative Coord	08	0303	GS	Vacant	DCI
Supply Technician	06	2005	GS	Shelton, W	DCI
Office Clerk	04	0326	GS	Franklin, AF	DCI

#### **RESEARCH OPERATIONS SERVICE**

<b>Description</b>	<b>Grade</b>	<b>MOS</b>	<b>Branch</b>	<b>Name</b>	<b>Activity</b>
Chief, Res Ops Svc	13	1320	GS	Abdel-Rahim, M	DCI
Immunologist	13	0401	GS	Zhou, Y	DCI
Bio Sci Lab Tech	O5	0404	GS	Martin, JL	DCI
Biochemist	O3	71B67	MS	Poore', D	DCI
Rsch Biologist	12	0401	GS	Vacant	DCI
Microbiologist	12	0403	GS	Vacant	DCI

Rsch Physiologist	12	0413	GS	Lukes, YD	DCI
Rsch Chemist	12	1320	GS	Nicholson, DE	DCI
Chemist	12	1320	GS	Vacant	DCI
Rsch Chemist	11	1320	GS	Bednarek, JM	DCI
Med Technologist	11	0644	GS	Kapur, JJ	DCI
Med Technologist	11	0644	GS	Morris, E	DCI
Med Technologist	11	0644	GS	Barnes, SG	DCI
Med Technologist	11	0644	GS	Anderson, JS	DCI
Med Technologist	11	0644	GS	Fileta, B	DCI
Bio Lab Tech	09	0404	GS	Reinhardt, B	DCI
Med Lab Spc	E4	91K10	NC	Rich, T	DCI
Med Lab Spc	E4	91K10	NC	Hoch, D	DCI
Med Lab Spc	E4	91K10	NC	Roberts, L	DCI

#### **CLINICAL STUDIES SERVICE**

<b>Description</b>	<b>Grade</b>	<b>MOS</b>	<b>Branch</b>	<b>Name</b>	<b>Activity</b>
Chief	O5	61P00	MC	Marin, R	DCI-Deployed-Iraq
Rsch Chemist	12	1320	GS	Maydonovitch, C	Gastroenterology
Nurse Specialist	12	0610	GS	Parchment, VA	DCI
Nurse Specialist	12	0610	GS	Bicknell, E	DCI
Other				Ocuin, E	Contract

E. Funding

	<b>FY 00</b>	<b>FY 01</b>	<b>FY 02</b>	<b>FY 03</b>
<b><u>Appropriated funding</u></b>				
Civilian personnel	\$2,177,569	\$2,292,958	\$2,102,400	\$2,245,931
Military personnel	418,699	419,691	516,194	515,961
Consumable supplies	256,972	257,780	212,000	126,750
Civilian contracts	319,200	332,000	417,683	368,981
TDY	47,727	47,000	47,000	50,497
Capital expense equipment program (CEEP)	0	0	0	72,271
MEDCASE	236,660	0	0	224,338
Operations	0	589,700	0	0
Infra-structure program	13,100	0	0	0
Subtotal	3,469,927	3,939,129	3,295,277	3,604,729
<b><u>Extramural funding</u></b>				
GOG	251,621	8,800	0	0
CALGB	99,188	24,253	23,945	23,247
VA	426,394	32,214	0	0
USUHS/DOD/MRMC	15,330,466	6,481,100	3,900,214	0
NIH/NCI	755,713	335,246	982,223	7,068,327
USUAMRMC	15,426	0	2,645,279	2,358,724
Partners Health Care System	8,320	0	0	0
Tri-Service nursing	445,781	409,924	0	0
Travel (non-federal sources)	21,626	38,292	0	0
Gifts (managed by DCI)	169,022	4,200	0	0

CRDAs (managed by DCI)	277,722	315,106	2,553,931	27,730
Royalty	14,400	0	0	35,473
SWOG	0	0	4,288	0
Other (DWHRP, etc.)	0	0	0	1,567,778
<hr/>				
<b>TOTAL</b>	21,285,606	11,588,264	13,405,157	14,686,008
<hr/>				



Financial Report On Protocols in FY2003  
By Department and Service

Department	Service	Protocol	Carry-In	Authorized	Expenses	Carry-Out
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*DENTAC*

9400-99	\$1,000	\$0	\$0	\$0
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<i>Department Total</i>	\$1,000	\$0	\$0	\$0
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*Department of Allergy-Immunology*

00-33003E	\$1,000	\$0	\$0	\$0
01-33001	\$1,000	\$0	\$0	\$0
02-33003	\$1,000	\$0	\$0	\$0
02-33005E	\$1,000	\$0	\$0	\$0
02-33006E	\$1,000	\$0	\$0	\$0
03-33004	\$0	\$1,000	\$836	\$0
03-33005	\$0	\$7,500	\$5,227	\$0
03-33007EX	\$0	\$1,000	\$0	\$1,000
03-33008EX	\$0	\$1,000	\$0	\$1,000
03-33010EX	\$0	\$1,000	\$0	\$1,000
03-33012EX	\$0	\$1,000	\$0	\$1,000

<i>Department Total</i>	\$5,000	\$12,500	\$6,063	\$4,000
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*Department of Clinical Investigation*

00-92003E	\$1,000	\$0	\$0	\$0
00-9201	\$1,000	\$0	\$0	\$0
01-92006E	\$1,000	\$0	\$0	\$0
9223-99	\$1,000	\$0	\$0	\$0

<i>Department Total</i>	\$4,000	\$0	\$0	\$0
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*Department of Medicine*

Cardiology Service

00-1201	\$1,000	\$0	\$0	\$1,000
01-12001	\$1,000	\$0	\$0	\$0
02-12007	\$0	\$1,500	\$144	\$0
02-12008	\$0	\$1,000	\$0	\$0
03-12004EX	\$0	\$1,000	\$0	\$1,000
Service Total	\$2,000	\$3,500	\$144	\$2,000

Dermatology Service

1828	\$1,000	\$0	\$0	\$0
Service Total	\$1,000	\$0	\$0	\$0

Endocrine Service

00-13003E	\$1,000	\$0	\$0	\$0
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Department	Service	Protocol	Carry-In	Authorized	Expenses	Carry-Out	
		00-1303	\$0	\$2,805	\$1,768	\$0	
		01-13004	\$1,000	\$0	\$0	\$0	
		01-13005	\$1,000	\$0	\$0	\$0	
		01-13008E	\$1,000	\$0	\$0	\$0	
		02-13006	\$0	\$5,450	\$3,778	\$1,000	
		02-13008	\$1,000	\$0	\$0	\$0	
		02-13009	\$1,000	\$0	\$0	\$1,000	
		02-13009E	\$1,000	\$0	\$0	\$0	
		02-13011	\$0	\$1,000	\$0	\$0	
		03-13012EX	\$0	\$1,000	\$0	\$1,000	
		03-13013	\$0	\$3,888	\$2,043	\$0	
		Service Total		\$7,000	\$14,143	\$7,589	\$3,000
	Gastroenterology Service						
	00-14001E	\$1,000	\$0	\$0	\$0		
	00-1403	\$0	\$1,000	\$0	\$1,000		
	00-1404	\$1,000	\$0	\$0	\$1,000		
	00-1406	\$1,000	\$0	\$0	\$0		
	01-14001	\$1,000	\$0	\$0	\$0		
	01-14003	\$0	\$1,000	\$723	\$0		
	01-14004	\$1,000	\$0	\$0	\$0		
	01-14005E	\$1,000	\$0	\$0	\$0		
	01-14006	\$1,000	\$0	\$0	\$1,000		
	02-14007	\$1,000	\$0	\$0	\$0		
	02-14008	\$0	\$1,000	\$0	\$0		
	02-14008E	\$1,000	\$0	\$0	\$0		
	02-14011	\$0	\$2,089	\$1,979	\$0		
	02-14012	\$1,000	\$0	\$0	\$0		
	02-14012E	\$0	\$1,000	\$723	\$0		
	02-14013	\$0	\$8,095	\$2,518	\$0		
	03-14013EX	\$0	\$1,000	\$0	\$1,000		
	03-14014	\$0	\$6,750	\$0	\$0		
	03-14014EX	\$0	\$1,000	\$0	\$1,000		
	03-14015EX	\$0	\$1,000	\$1,024	\$0		
	03-14017	\$0	\$2,200	\$900	\$0		
	03-14019	\$0	\$1,048	\$0	\$0		
	Service Total		\$10,000	\$27,182	\$7,867	\$5,000	
General Medicine Service							
	00-10001E	\$1,000	\$0	\$0	\$0		
	00-1001	\$1,000	\$0	\$0	\$0		
	02-10004	\$0	\$1,000	\$0	\$0		
	02-10011E	\$1,000	\$0	\$0	\$1,000		
	02-10012E	\$0	\$1,000	\$0	\$0		
	03-10014EX	\$0	\$1,000	\$0	\$1,000		
	03-10017EX	\$0	\$0	\$0	\$1,000		
	03-13011EX	\$0	\$1,000	\$0	\$1,000		
	1060-99	\$1,000	\$0	\$0	\$1,000		
	Service Total		\$4,000	\$4,000	\$0	\$5,000	
Hematology-Oncology Service							
	00-1605	\$1,000	\$0	\$0	\$1,000		
	01-16002	\$1,000	\$0	\$0	\$1,000		

Department	Service	Protocol	Carry-In	Authorized	Expenses	Carry-Out
Infectious Disease Service		02-16000E	\$1,000	\$0	\$0	\$1,000
	Service Total		\$3,000	\$0	\$0	\$3,000
		02-19002E	\$0	\$1,000	\$1,000	\$0
		03-19005EX	\$0	\$1,000	\$0	\$1,000
		03-19006	\$0	\$1,000	\$0	\$0
		03-19006EX	\$0	\$1,000	\$507	\$0
		03-19007	\$0	\$1,000	\$0	\$0
		03-19007EX	\$0	\$1,000	\$0	\$1,000
		1903-98	\$0	\$2,500	\$1,731	\$0
		1993	\$0	\$1,000	\$0	\$0
	Service Total		\$0	\$9,500	\$3,238	\$2,000
Nephrology Service		00-1101	\$1,000	\$0	\$0	\$0
		00-11011E	\$1,000	\$0	\$0	\$0
		00-1102	\$1,000	\$0	\$0	\$1,000
		01-11002	\$1,000	\$0	\$0	\$1,000
		02-11004	\$1,000	\$0	\$0	\$0
		02-11005	\$1,000	\$0	\$0	\$0
		03-11006	\$0	\$1,000	\$0	\$0
		03-11013EX	\$0	\$1,000	\$952	\$0
		03-11016EX	\$0	\$1,000	\$0	\$1,000
		1197-99	\$1,000	\$0	\$0	\$1,000
		1198-99	\$1,000	\$0	\$0	\$0
		1199-99	\$1,000	\$0	\$0	\$1,000
	Service Total		\$9,000	\$3,000	\$952	\$5,000
Pulmonary & Critical Care Medicine Service		01-17005	\$1,000	\$0	\$0	\$0
		01-17006	\$1,000	\$0	\$0	\$0
		01-17006E	\$1,000	\$0	\$810	\$0
		01-17007E	\$1,000	\$0	\$0	\$0
		01-17009E	\$1,000	\$0	\$0	\$0
		01-1701	\$1,000	\$0	\$0	\$0
		01-17010E	\$0	\$1,000	\$1,000	\$0
		01-17013E	\$1,000	\$0	\$0	\$0
		01-17014E	\$1,000	\$0	\$0	\$0
		02-17008	\$1,000	\$0	\$0	\$0
		02-17009	\$0	\$7,630	\$0	\$0
		02-17012	\$0	\$1,000	\$0	\$0
		02-17013	\$0	\$2,000	\$0	\$0
		02-17014	\$0	\$1,000	\$0	\$0
		02-17016E	\$1,000	\$0	\$0	\$0
		02-17016EX	\$1,000	\$0	\$0	\$0
		02-17017E	\$0	\$1,000	\$0	\$0
		02-17018E	\$1,000	\$0	\$0	\$0
		02-17020E	\$0	\$1,000	\$0	\$0
		02-17021E	\$0	\$1,000	\$0	\$0
		03-17015	\$0	\$1,000	\$0	\$0
		03-17021EX	\$0	\$1,000	\$0	\$1,000
	Service Total		\$12,000	\$17,630	\$1,810	\$1,000

Department	Service	Protocol	Carry-In	Authorized	Expenses	Carry-Out
Rheumatology Service						
		00-3701	\$1,000	\$0	\$0	\$0
		00-3702	\$1,000	\$0	\$0	\$0
		01-37001	\$1,000	\$0	\$0	\$1,000
	Service Total		\$3,000	\$0	\$0	\$1,000
	<i>Department Total</i>		\$51,000	\$78,955	\$21,600	\$27,000

### *Department of Neurology*

	00-7102	\$1,000	\$0	\$0	\$1,000
	01-71001	\$1,000	\$0	\$0	\$0
	02-71005	\$0	\$1,000	\$0	\$0
	02-71006	\$1,000	\$0	\$0	\$1,000
	02-71011	\$0	\$1,000	\$0	\$0
	03-71014	\$0	\$1,000	\$0	\$0
	03-71018	\$0	\$1,000	\$0	\$0
	7176-99	\$1,000	\$0	\$0	\$0
	<i>Department Total</i>	\$4,000	\$4,000	\$0	\$2,000

### *Department of Nursing*

	02-75014E	\$1,000	\$0	\$0	\$0
	<i>Department Total</i>	\$1,000	\$0	\$0	\$0

### *Department of Obstetrics and Gynecology*

	00-44007E	\$1,000	\$0	\$0	\$0
	00-44009E	\$1,000	\$0	\$0	\$0
	00-44010E	\$1,000	\$0	\$0	\$0
	00-44011E	\$1,000	\$0	\$0	\$0
	00-4403	\$1,000	\$0	\$0	\$0
	00-4404	\$1,000	\$0	\$0	\$1,000
	00-4406	\$1,000	\$0	\$617	\$0
	01-44002	\$1,000	\$0	\$0	\$0
	01-44005	\$1,000	\$0	\$0	\$1,000
	01-44016E	\$1,000	\$0	\$0	\$0
	01-44018E	\$1,000	\$0	\$0	\$0
	02-44021E	\$0	\$1,000	\$0	\$0
	03-44023EX	\$0	\$1,000	\$0	\$1,000
	03-44024EX	\$0	\$1,000	\$0	\$1,000
	03-44026EX	\$0	\$1,000	\$0	\$1,000
	03-44027EX	\$0	\$1,000	\$0	\$1,000
	44005E99	\$1,000	\$0	\$0	\$0
	4413-99	\$1,000	\$0	\$0	\$1,000
	<i>Department Total</i>	\$13,000	\$5,000	\$617	\$7,000

Department	Service	Protocol	Carry-In	Authorized	Expenses	Carry-Out
<i>Department of Orthopaedics and Rehabilitation</i>						
Orthopedics Surgery Service						
		00-24007E	\$1,000	\$0	\$0	\$0
		00-24008E	\$1,000	\$0	\$0	\$0
		00-2401	\$0	\$1,000	\$0	\$0
		00-24010E	\$1,000	\$0	\$0	\$0
		00-2402	\$1,000	\$0	\$0	\$0
		00-2404	\$1,000	\$0	\$0	\$0
		00-2406	\$1,000	\$0	\$0	\$0
		01-24003	\$1,000	\$0	\$914	\$0
		01-24004	\$1,000	\$0	\$0	\$0
		01-24005	\$1,000	\$0	\$0	\$1,000
		01-24008	\$1,000	\$0	\$0	\$1,000
		01-24009	\$1,000	\$0	\$914	\$0
		01-2401	\$0	\$1,000	\$0	\$0
		01-24010	\$1,000	\$0	\$998	\$0
		01-24015E	\$1,000	\$0	\$0	\$0
		01-2402	\$1,000	\$0	\$0	\$1,000
		02-24012	\$1,000	\$0	\$0	\$0
		02-24013	\$0	\$1,000	\$998	\$0
		02-24014	\$1,000	\$0	\$0	\$0
		02-24015	\$1,000	\$0	\$0	\$0
		02-24017E	\$1,000	\$0	\$0	\$0
		02-24018	\$0	\$1,000	\$0	\$0
		02-24019E	\$1,000	\$0	\$0	\$0
		02-24020	\$0	\$6,000	\$0	\$0
		02-24020E	\$0	\$1,000	\$565	\$0
		02-24021E	\$1,000	\$0	\$0	\$0
		02-24022EX	\$0	\$1,000	\$565	\$0
		02-24023E	\$0	\$1,000	\$0	\$0
		03-24021	\$0	\$2,600	\$720	\$0
		03-24024EX	\$0	\$1,000	\$0	\$1,000
		03-24025	\$0	\$1,000	\$0	\$0
		03-24025EX	\$0	\$1,000	\$0	\$1,000
		03-24027	\$0	\$1,164	\$0	\$0
		03-24028	\$0	\$1,433	\$0	\$0
		2410-99	\$0	\$1,000	\$0	\$0
	Service Total		\$20,000	\$22,197	\$5,674	\$5,000
Physical Medicine & Rehabilitation Service						
		00-96002E	\$1,000	\$0	\$0	\$0
		00-96003E	\$1,000	\$0	\$0	\$0
		00-9601	\$1,000	\$0	\$0	\$0
		00-9602	\$1,000	\$0	\$0	\$1,000
		00-9603	\$1,000	\$0	\$0	\$0
		00-9604	\$1,000	\$0	\$0	\$0
		01-24014E	\$1,000	\$0	\$0	\$0
		01-96009E	\$1,000	\$0	\$0	\$0
		02-96006	\$0	\$1,000	\$949	\$0
		02-96010E	\$1,000	\$0	\$0	\$0
		03-96008	\$0	\$395	\$395	\$0
		03-96011EX	\$0	\$1,000	\$0	\$1,000

Department	Service	Protocol	Carry-In	Authorized	Expenses	Carry-Out
		03-96012EX	\$0	\$1,000	\$0	\$1,000
		03-96013EX	\$0	\$1,000	\$0	\$1,000
	Service Total		\$9,000	\$4,395	\$1,344	\$4,000
	<i>Department Total</i>		\$29,000	\$26,592	\$7,018	\$9,000

### *Department of Pediatrics*

00-64005E	\$1,000	\$0	\$0	\$0
00-6501	\$1,000	\$0	\$0	\$0
00-6503	\$1,000	\$0	\$0	\$0
00-6504	\$1,000	\$0	\$0	\$1,000
01-64007E	\$1,000	\$0	\$0	\$0
01-64008E	\$1,000	\$0	\$0	\$0
01-65001a	\$1,000	\$0	\$0	\$1,000
01-65001b	\$0	\$5,700	\$4,557	\$0
01-65002	\$1,000	\$0	\$0	\$0
02-65001d	\$0	\$5,850	\$0	\$0
02-65001EX	\$1,000	\$0	\$0	\$0
02-65005	\$0	\$2,750	\$2,738	\$0
02-65007	\$1,000	\$0	\$0	\$0
03-14017EX	\$0	\$1,000	\$1,062	\$0
03-66004	\$0	\$4,000	\$0	\$0
6430-99	\$1,000	\$0	\$0	\$0

*Department Total* \$11,000 \$19,300 \$8,357 \$2,000

### *Department of Pharmacy*

00-36003E	\$1,000	\$0	\$0	\$0
03-36005EX	\$0	\$1,000	\$1,000	\$1,000

*Department Total* \$1,000 \$1,000 \$1,000 \$1,000

### *Department of Psychiatry*

00-72005E	\$1,000	\$0	\$0	\$0
00-7201	\$1,000	\$0	\$0	\$0
02-72004	\$0	\$1,000	\$0	\$0
02-72007E	\$1,000	\$0	\$0	\$0
02-72009E	\$1,000	\$0	\$0	\$0
7284-99	\$1,000	\$0	\$0	\$0

*Department Total* \$5,000 \$1,000 \$0 \$0

### *Department of Psychology*

01-73002E	\$1,000	\$0	\$0	\$0
02-73003E	\$1,000	\$0	\$0	\$0

Department	Service	Protocol	Carry-In	Authorized	Expenses	Carry-Out
		02-73004	\$0	\$1,000	\$0	\$0
		02-73005E	\$1,000	\$0	\$0	\$0
	<i>Department Total</i>		\$3,000	\$1,000	\$0	\$0
<i>Department of Radiology</i>						
	Diagnostic Radiology Service					
		01-47002	\$1,000	\$0	\$0	\$1,000
		01-4701	\$0	\$1,000	\$0	\$0
		4710-99	\$1,000	\$0	\$0	\$1,000
	Service Total		\$2,000	\$1,000	\$0	\$2,000
	Nuclear Medicine Service					
		00-4501	\$1,000	\$0	\$0	\$0
		01-45000E	\$1,000	\$0	\$0	\$0
		01-4501	\$1,000	\$0	\$0	\$1,000
		02-45005	\$0	\$1,000	\$0	\$0
	Service Total		\$3,000	\$1,000	\$0	\$1,000
	Radiation Therapy					
		01-46001	\$1,000	\$0	\$0	\$1,000
	Service Total		\$1,000	\$0	\$0	\$1,000
	<i>Department Total</i>		\$6,000	\$2,000	\$0	\$4,000
<i>Department of Surgery</i>						
	Anesthesia-Operative Service					
		00-2002A	\$1,000	\$0	\$0	\$0
		01-20002A	\$1,000	\$0	\$0	\$0
		01-2001A	\$1,000	\$0	\$0	\$1,000
		01-31001E	\$1,000	\$0	\$0	\$0
		03-31005EX	\$0	\$1,000	\$0	\$1,000
	Service Total		\$4,000	\$1,000	\$0	\$2,000
	Army Audiology & Speech Center					
		02-25005	\$0	\$1,000	\$949	\$0
	Service Total		\$0	\$1,000	\$949	\$0
	Critical Care Medicine Service					
		02-30000E	\$1,000	\$0	\$1,000	\$0
		02-30003	\$1,000	\$0	\$0	\$1,000
		3002-99	\$1,000	\$0	\$0	\$0
	Service Total		\$3,000	\$0	\$1,000	\$1,000
	General Surgery Service					
		00-2001	\$1,000	\$0	\$0	\$1,000
		00-2003	\$1,000	\$0	\$0	\$1,000
		01-20005	\$1,000	\$0	\$0	\$0
		02-20008	\$0	\$1,000	\$0	\$0
		02-27000E	\$1,000	\$0	\$0	\$0
		02-31002E	\$1,000	\$0	\$0	\$0
		03-20006EX	\$0	\$1,000	\$733	\$1,000
		03-20010	\$0	\$6,000	\$0	\$0

Department	Service	Protocol	Carry-In	Authorized	Expenses	Carry-Out
Ophthalmology Service		03-20015	\$0	\$1,000	\$0	\$0
		03-27001EX	\$0	\$1,000	\$0	\$1,000
		2080-99	\$1,000	\$0	\$0	\$0
	Service Total		\$6,000	\$10,000	\$733	\$4,000
		00-2302	\$1,000	\$0	\$0	\$0
		01-23001	\$1,000	\$0	\$0	\$1,000
		03-23002	\$0	\$1,000	\$0	\$0
		2335-99	\$1,000	\$0	\$0	\$0
	Service Total		\$3,000	\$1,000	\$0	\$1,000
		01-26002E	\$1,000	\$0	\$0	\$0
Organ Transplant Service	Service Total		\$1,000	\$0	\$0	\$0
Otolaryngology-Head & Neck Surgery Service						
		00-2504	\$1,000	\$0	\$0	\$0
		00-2509	\$1,000	\$0	\$0	\$0
		01-32004	\$1,000	\$0	\$0	\$1,000
		01-3202	\$1,000	\$0	\$0	\$1,000
		02-25002E	\$1,000	\$0	\$0	\$0
		02-25003E	\$1,000	\$0	\$0	\$0
		02-32009	\$1,000	\$0	\$0	\$1,000
		03-32012	\$0	\$1,000	\$0	\$0
		03-32014	\$0	\$8,501	\$7,500	\$0
	Service Total		\$7,000	\$9,501	\$7,500	\$3,000
Peripheral Vascular Surgery Service						
		00-2101	\$1,000	\$0	\$0	\$1,000
		00-2102	\$1,000	\$1,500	\$1,319	\$0
		01-2101	\$0	\$1,000	\$0	\$0
		02-21001E	\$1,000	\$0	\$1,000	\$0
		02-21002	\$0	\$6,000	\$0	\$1,000
		03-21001EX	\$0	\$1,000	\$0	\$1,000
		03-21003	\$0	\$1,000	\$0	\$0
		2125	\$0	\$1,000	\$978	\$0
		2130-99	\$0	\$6,860	\$7,055	\$0
	Service Total		\$3,000	\$18,360	\$10,352	\$3,000
Urology Service						
		00-28004E	\$1,000	\$0	\$0	\$0
		01-28004	\$1,000	\$0	\$0	\$0
		03-28008EX	\$0	\$1,000	\$0	\$1,000
		03-28022	\$0	\$7,460	\$0	\$0
		2890-99	\$1,000	\$0	\$0	\$1,000
		2891-99	\$1,000	\$0	\$0	\$0
		2894-99	\$1,000	\$0	\$0	\$0
	Service Total		\$5,000	\$8,460	\$0	\$2,000
<i>Department Total</i>			\$32,000	\$49,321	\$20,534	\$16,000



Department	Service	Protocol	Carry-In	Authorized	Expenses	Carry-Out
<i>Deployment Health Clinical Center</i>						
		00-89001E	\$1,000	\$0	\$0	\$0
	<i>Department Total</i>		\$1,000	\$0	\$0	\$0
<i>DeWitt Army Hospital</i>						
		00-83001E	\$1,000	\$0	\$0	\$0
	<i>Department Total</i>		\$1,000	\$0	\$0	\$0
<i>Fort Belvoir, VA</i>						
		01-83001	\$1,000	\$0	\$0	\$0
	<i>Department Total</i>		\$1,000	\$0	\$0	\$0
	<b>GRAND TOTAL</b>		<b>\$169,000</b>	<b>\$200,668</b>	<b>\$65,189</b>	<b>\$72,000</b>

F. Research activity accomplished in FY 03

With the mission to empower WRAMC researchers from planning to publication, the Department of Clinical Investigation (DCI) supported a total of 952 active protocols this year (see Table I.).

Two hundred and fifty-five of these studies were newly approved during the fiscal year. The remaining 697 studies were ongoing during the previous fiscal year.

**Table I. - WRAMC protocol activity**

Protocols	FY00	FY01	FY02	FY03
Ongoing at beginning of FY	646	680	675	697
Newly approved (+)	196	222	248	255
(Full protocols)	(129)	(155)	(169)	(150)
(Exempt protocols)	(67)	(67)	(79)	(105)
Total active during FY	842	902	923	952
Closed (-)	144	214	218	251
(Full protocols)	(144)	(139)	(151)	(107)
(Exempt protocols)	(0)	(75)	(67)	(144)
Terminated (-)	10	7	2	4
Withdrawn (-)	8	6	6	17
Ongoing at end of FY	680	675	697	680

In FY 03, the Human Use Committee (HUC) and/or the Clinical Investigation Committee (CIC) approved a total of 255 new protocols, including the exempt protocols granted. The procedure established for exempt category protocols was continued, whereby human use research that does not fall within the purview of the Human Use Committee/Institutional Review Board (HUC/IRB) is reviewed within DCI to determine if it meets exempt criteria. A total of 105 new protocols were granted exemption in FY 03.

In addition to administering the initial review and approval of new protocols, the continuing review of the ongoing protocols is also administrated by the Department of Clinical Investigation (DCI), Research Review Service (RRS). Continuing review of ongoing approved protocols was conducted prior to or during the anniversary month of the original approval of the protocols. In order to ensure timely completion, a request is sent to the principal investigator for submission of an annual progress report (APR) two months preceding the

month the APR is actually due. The completed report consists of a detail summary sheet (DSS), a list of publications for the research resulting from the protocol, a copy of the approved consent form, a questionnaire regarding the maintenance of research records, and the continuing review of human subject participation or animal use. Human Use Committee members serve as primary reviewers for the annual progress reports. Their recommendations are presented to the HUC/IRB for their final review and vote. A total of 556 annual progress reports were reviewed and approved. Failure to submit an APR within sixty days after the anniversary date of the protocol results in administrative termination by the HUC, and investigators are informed that no research may be published. The Institutional Biosafety Committee continued to review three active gene therapy protocols during FY 03.

The RRS also performs and coordinates with CSS regarding other protocol regulatory activities, including addenda, audit reports, and adverse events reporting. Table II provides a summary of all the ongoing activities for FY 00 to FY 03.

**Table II. - WRAMC other research review activity**

	FY00	FY01	FY02	FY03
Continuing Review and Approval of Annual Progress Reports	539	516	549	556
Addenda Reviewed	266	217	200	214
Audits Conducted	33	37	52	51
Adverse Events Reported	539	329	503	629

Publication and presentation activities by WRAMC staff are listed in Table III for FY 00 to FY 03. Detailed information of these activities in FY 03 is listed beginning on page 87 of Volume I for each department and service.

**Table III. - WRAMC publications, abstracts and presentations**

	FY00	FY01	FY02	FY03
Publications	349	370	446	467
Abstracts	121	99	346	334
Presentations	584	564	588	766
Other				4
TOTAL	1,054	1,033	1,380	1,571

The RRS maintained and updated the "Principal Investigator's Guide" which explains the research review process, details research resources available at WRAMC, and provides checklists, formats, and guidelines for principal investigators. The "Principal Investigator's Guide" and the routine forms and instructions necessary for preparation of a protocol application are available through the DCI website at [www.wramc.amedd.army.mil/departments/dci](http://www.wramc.amedd.army.mil/departments/dci).

The Biometrics Section of the RRS continued to provide a wide range of statistical support to investigators including research design, sample size estimation, data analysis, and general troubleshooting. Three levels of statistical courses were offered to the investigators regarding how to conduct data analyses using the SPSS program. Course contents included data coding, data entry, common statistical methods for data analysis, and non-parametric statistics. The Biometrics Section remained vital in facilitating and enhancing the functions and capabilities of research data analysis at WRAMC.

The Research Operations Service (ROS), under the direction of Mr. Maged Abdel-Rahim, completed the relocation of the laboratories and offices from Building T-2 to Building 7. The ROS maintained its support to the research initiative at WRAMC and the graduate medical education by providing technical expertise in the areas of immunology, molecular biology, biochemistry, and experimental pathology. The ROS successfully filled two of the vacant positions of Immunologist, Dr. Yaling Zhou, and a Medical Technologist, Mr. Brian Reinhardt. Dr. Zhou's expertise will expand the ability of the ROS to conduct studies in the area of cell biology and immunology. With the availability of individual expertise and sophisticated equipment, the ROS can support the research efforts at WRAMC in both genomic and proteomic fields.

The Research Administration Service (RAS), under the direction of Ms. Daisy Word, provided administrative support to the Department and to WRAMC investigators. Support to investigators was in the form of preparation of research-related TDY and accountability of study funds. RAS also oversees the computer laboratory section. In FY 03, DCI received 307 new protocols. Of this number, RAS managed intramural funds for 114 protocols (37%) and reviewed and processed Cooperative Research and Development Agreements (CRDAs) for 29 studies (9%). The remaining studies were either funded by federal grants, cooperative oncology groups, or required no funding. The grant and CRDA documents were initially reviewed and approved at WRAMC and forwarded to CIRO and intermediary organizations. Disbursement of funds was managed almost exclusively by the intermediary organizations. The major sources of extramural funding included U.S. Army Medical Research and Materiel Command, National Institutes of Health, and Cancer and Leukemia Group B. CRDA funds, largely from pharmaceutical and technology companies, were managed by the Henry M. Jackson Foundation for the Advancement of Military Medicine (HMJF), the T.R.U.E. Foundation, and the Geneva Foundation.

The Computer Operations Section of RAS continued its refinement of the comprehensive database for thousands of research records encompassing several years. Phase I was completed, which monitors details of each protocol from submission to IRB approval. Phase II will cover continuing review documents (APRs, adverse events, publication clearances, etc.), and was approximately 50% completed. The initial stage was also begun for electronic protocol review by the CIC and the IBC.

The Clinical Studies Service (CSS), under the direction of LTC Raul Marin MC, continued to serve as the conduit of educational efforts to the WRAMC investigator community regarding all aspects of research. Among the educational courses offered were the DCI Research Course (web-based), the DCI Research Refresher Course (web-based), the Research in Clinical Medicine Course (live), the HIPAA and Research Lecture Series, and numerous other individual lectures that can be found in the DCI web page. The CSS was also responsible for the DCI Protocol Audit Program, the management of adverse events reported to the WRAMC HUC, publication clearance, and the administration of the Bailey K. Ashford Clinical and Laboratory Research Symposium and Awards.

Under the auspices of the WRAMC Professional Education and Training Committee, DCI continued to provide training for WRAMC personnel regarding research regulations and the conduct of research at

WRAMC. The web-based WRAMC research course continues to be available on-line for initial and continuing research training of investigators. This on-line availability facilitated timely completion of the required course for researchers who come to WRAMC throughout the year.

The 29th Annual Bailey K. Ashford Clinical and Laboratory Research Awards were bestowed on members of the 2003 graduating class whose research accomplishments excelled during training. The selection committee chose eight finalists from the thirty-four nominations. The finalists presented their research results at a symposium on 1 May 2003 sponsored by Department of Clinical Investigation. The winners in the clinical and laboratory research categories and the finalists, along with their presentation topics, appear in Volume I. A poster session was held the morning of the symposium to allow the other nominees an opportunity to present their work to the WRAMC community.

The Department of Clinical Investigation received the active support of many WRAMC staff members via their participation on the Human Use Committee/Institutional Review Board (HUC/IRB -- Tables IV. and V.), the Clinical Investigation Committee (CIC -- Tables VI. and VII.), and the Institutional Biosafety Committee (IBC -- Table VIII.). The research expertise of these individuals contributed significantly to the scientific rigor of the WRAMC clinical investigation program.

**Table IV. - Human Use Committee/Institutional Review Board Primary Members for FY 03**

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**Chairpersons HUC**

COL James Kikendall, MC+	Gastroenterology Service DOM, Rep DCCS
COL Christina Yuan, MC+	Nephrology Service DOM, Rep DCCS
LTC Raul Marin, MC	Co-Chairperson, HUC DCI, Assistant Chief
Audrey Chang, Ph.D. DAC	Co-Chairperson, HUC DCI, Research Review Service, Chief
+ Alternate chairing of the HUC meetings	

**WRAMC Members**

David Gillespie, LTC, MC	Peripheral Vascular Surgery Service (Rep) Chief, Department of Surgery
Teresa Kemmer, LTC, SP	(Rep) Chief, Nutrition Care Directorate
E. Wayne Combs, LTC, AN	(Rep) Chief, Department of Nursing
Aubrey Waddell, LTC, MS	(Rep) Chief, Department of Pharmacy
Geoffrey Grammer, MAJ, MC	(Rep) Chief, Department of Psychiatry
William Sager, MAJ, CH	(Rep) Chief, Dept of Ministry and Pastoral Care
Laurel Meaney, DAC	Patients' Rights Representative
Scott Murdoch, JD, DAC	(Rep) Center Judge Advocate
Edward Bartlett, Ph.D, DAC	IRB Administrator Department of Clinical Investigation
Vicki Miskovsky, DAC	Recorder, HUC, Research Review Service Department of Clinical Investigation
Verna Parchment, RN, MS, DAC	Research Review Service Department of Clinical Investigation
Noah Schenkman, LTC, MC	Urology Service (Rep) Chief, Department of Surgery
Andrew Eiseman, LTC, MC	Ophthalmology Service (Rep) Chief, Department of Surgery

**Non-Affiliated Members**

George Tsokos, COL, MC	Department of Rheumatology, WRAIR
David Keyser, LCDR, MS	Military & Emergency Medicine
Richard Conran, COL, MC with Alan Fix, MD, MS, CIV (alternate)	Department of Pathology, USUHS NIAID - NIH
Bruce Schoneboom, LTC AN with Ruth Bulger, Ph.D., DOD (alternate)	Department of Nursing, USUHS Department of Anatomy, USUHS

**Table V. - Human Use Committee/Institutional Review Board Alternate Members for FY 03**

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Audrey Chang, Ph.D., DAC	Chief, Research Review Service, DCI Co-Chairperson, HUC
Raul Marin, LTC, MC	Assistant Chief (deployed), DCI Co-Chairperson, HUC
Alexander Stojadinovic, MAJ, MC	General Surgery Service (Rep) Chief, Department of Surgery
Patricia Patrician, LTC, AN	(Rep) Chief, Nursing Research Service
Deborah Kenny, LTC, AN	(Rep) Chief, Nursing Research Service
Dean Inouye, LTC, MC	(Rep) Chief, Department of Psychiatry
Irone Green, DAC	Research Review Service, DCI Recorder
George Peoples, Jr., LTC, MC	General Surgery Service (Rep) Chief, Department of Surgery
Karen Geisler, LTC, SP	(Rep), Chief, Nutrition Care Directorate



**Table VI. - Clinical Investigation Committee Primary Members for FY 03**

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Maria Sjogren, COL, MC	Chairperson, CIC Chief, Department of Clinical Investigation
Raul Marin, LTC, MC	Chairperson, CIC (deployed) Asst. Chief, Department of Clinical Investigation
Edward Bartlett, Ph.D, DAC	IRB Administrator Department of Clinical Investigation
Patricia Patrician, LTC(P), AN	(Rep) Chief, Nursing Research Service
Scott Murdoch, JD, DAC	(Rep) Center Judge Advocate
Audrey Chang, Ph.D., DAC	Chief, Research Review Service, DCI
Maged Abdel-Rahim, DAC	Chief, Research Operations Service, DCI
Daisy Word, MHSA, DAC	Chief, Research Administration Service, DCI
Noah Schenkman, LTC, MC	(Rep) Chief, Department of Surgery
Houman Tavaf, MAJ, MC	(Rep) Chief, Department of Surgery
Andrew Eiseman, MAJ, MC	(Rep) Chief, Department of Surgery

**Table VII. - Clinical Investigation Committee Alternate Members for FY 03**

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Erin Bohen, LTC, MC	(Rep) Chief, Department of Medicine
Scott Norton, LTC, MC	(Rep) Chief, Department of Medicine
Patrick O'Malley, LTC, MC	(Rep) Chief, Department of Medicine
Allen Taylor, LTC, MC	(Rep) Chief, Department of Medicine
Darren Baroni, MAJ, MC	(Rep) Chief, Department of Medicine
Andrew Shorr, MAJ, MC	(Rep) Chief, Department of Medicine
Jamie Waselenko, MAJ, MC	(Rep) Chief, Department of Medicine
Carl Willis, MAJ, MC	(Rep) Chief, Department of Medicine
Glenn Wortmann, MAJ, MC	(Rep) Chief, Department of Medicine
Beth Shultz-Butilus, CPT, MC	(Rep) Chief, Department of Medicine
Jonathan Roebuck, CPT, MC	(Rep) Chief, Department of Medicine

Derek Stocker, CPT, MC	(Rep) Chief, Department of Medicine
Thomas Burklow, LTC, MC	Department of Pediatrics
H. Joel Schmidt, COL, MC	Department of Pediatrics
Russell Moores, COL, MC	Department of Pediatrics
Andrew Bauer, MAJ, MC	Department of Pediatrics
Michelle Kravitz, MAJ, MC	Department of Pediatrics
Megan O'Brien, CPT, MC	Department of Pediatrics
Karla Auyeung, MAJ, MC	Department of Pediatrics
Steven Spencer, MAJ, MC	Department of Pediatrics
Maureen Petersen, CPT, MC	Department of Pediatrics
Margaret Swanberg, MAJ, MC	Department of Neurology
David Bartoszek, LTC, MC	Department of Neurology
Laurie Ryan, Ph.D., DOD	Department of Neurology
Deborah Kenny, LTC, AN	(Rep) Chief, Department of Nursing
Veronica Thurmond, LTC, AN	(Rep), Chief, Department of Nursing
Robin Howard, MS, DAC	Research Review Service, DCI
Francois Tuamokumo, Ph.D., DAC	Research Review Service, DCI
Roscoe Brunson, DAC	Research Administrations, DCI
Diarmuid Nicholson, Ph.D., DAC	Research Operations Service, DCI
Daniel Winand, JD, DAC	Center Judge Advocate
Christie Stewart, HJMF	Recorder, CIC

**Table VIII. - Institutional Biosafety Committee Board Members for FY 03**

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**WRAMC Affiliated Members**

COL Craig D. Shriver, MC	Assistant Chair, General Surgery
LTC Thomas R. Burklow, MC	Pediatric Cardiology
LTC Raul Marin, MC	Physical Medicine & Rehab/Research Admin.
COL Bryan L. Martin, MC	Allergy/Immunology
Dr. Diarmuid Nicholson (Ph.D.)	Biochemistry/Molecular Biology
MAJ Paula Doulaveris, MS	Pharmacology
LTC Joel Fishbain, MC	Infectious Disease

**Non-Affiliated Members**

LTC Kent E. Kester, MC	Chair, Infectious Disease, WRAIR
COL Naomi E. Aronson, MC	Infectious Disease, USUHS
Dr. Kuan-Teh Jeang (MD, Ph.D.)	Molecular Virology, NIH
Dr. Shyh-Ching Lo, (MD, Ph.D.)	Molecular Pathobiology, AFIP
Ms. Donna J. Mateski (MS, RD)	Research Administration, Kaiser

**DCI Administration (non-voting)**

COL Maria H. Sjogren, MC	Chief, Dept. of Clinical Investigation
Dr. Audrey Chang (Ph.D.)	Chief, Research Review Service, DCI
CPT Duke Poore, MS	Clinical Studies Service, DCI
Ms. Michelle Porter (RN, MA)	Nurse Specialist
Dr. Edward Bartlett (Ph.D.)	Asst. Chief, Research Review Service, DCI

G. Research activity planned for FY 04

During FY 04 we will continue training all new principal investigators at WRAMC concerning the conduct of good clinical research through a one-day live research course or a six-hour self-taught web-based course. The Professional and Education Training Committee at WRAMC advises that all researchers are required to take a web-based refresher course after three years following the initial training course. We will continue to participate in the multi-institution oncology trials in the National Capital Area sponsored by the United States Military Cancer Institute (USMCI). The institutions that will be involved are National Navy Medical Center, Bethesda, MD, Malcolm Grow Medical Center, Andrews AFB, Uniformed Services University of Health Sciences, Bethesda, MD, and Walter Reed Army Medical Center, Washington, DC. Since efforts towards developing the Standard Operating Procedures for the Institutional Review Board (IRB) of the USMCI were successful, the Clinical Investigation Regulatory Office (CIRO) has approved it as a second WRAMC IRB and this will also be incorporated to the WRAMC Federal Wide Assurance. The principal investigators may submit their protocols to the USMCI when the research studies involve more than Walter Reed Army Medical Center as a study site. A multi-site tissue banking protocol will be submitted to the WRAMC DCI for consideration of USMCI funding.

The major focus in FY 04 will be to streamline the review and approval process and to conduct timely review and approval for war-related studies that will potentially contribute to the health care of the soldiers at war or stationed overseas. In addition, DCI will continue to ensure the compliance of the Health Insurance Portability and Accountability Act (HIPAA) for WRAMC research protocols. The HIPAA regulations apply to all ongoing protocols that are still enrolling research participants and to all applicable new protocols.

Research is an ever growing and challenging enterprise. For FY04, we will continue to apply the WRAMC Tissue Banking Policy and Guidelines to ensure that the patient confidentiality is well protected and to implement (or adapt) other new requirements, particularly with respect to gene therapy regulations. Trainings of members of the Institutional Review Boards, both CIC and HUC, and the members of the Institutional Biosafety Committee (IBC) will continue. Our IBC will meet quarterly to actively review and oversee the biosafety issues of two existing gene therapy protocols. DCI will continue to update and guide WRAMC investigations so that the best protection program for research volunteers is implemented.

H. The Bailey K. Ashford Clinical and Laboratory Research Symposium – FY 03

**LABORATORY AND CLINICAL PRESENTATION AND POSTER FINALISTS**

**First Place - Laboratory Award Category**

MAJ Charles Fox, MC (Chief Resident, General Surgery)  
“Praj-1 is Linked to the Insulin Like Growth Factor-1 Mediated Protein Kinase B/Akt Signaling Pathway in Atherosclerosis”

**First Place - Clinical Research Award Category**

MAJ Scott Shawen, MC (Chief Resident, Orthopaedic Surgery)  
“Osteoporosis and Anterior Femoral Notching in Periprosthetic Femur Fractures: A Biomechanical Analysis”

**First Place - Laboratory Poster Award Category**

MAJ Steven Spencer, MC (Fellow, Pediatric Infectious Disease)  
“Topical Microbicides Inhibit GC Infection in a Novel Mouse Model”

**First Place - Clinical Research Poster Award Category**

CPT Russell Peckham, MC (Resident, Internal Medicine)  
“Potential Limitations of Clinical Criteria for the Diagnosis of Idiopathic Pulmonary Fibrosis”

**RESEARCH PRESENTATION FINALISTS**

**Laboratory Research Award Category**

MAJ Charles Fox MC (Resident, General Surgery Service)  
CPT Sean Montgomery MC (Resident, General Surgery Service)  
LCDR Richard Ruck, USN, MC (Resident, Department of Pediatrics)  
MAJ Kenneth Taylor MC (Resident, Orthopaedic Surgery Service)

**Clinical Research Award Category**

MAJ Scott Shawen MC (Resident, Orthopaedic Surgery Service)  
MAJ Philip Belmont MC (Resident, Orthopaedic Surgery Service)  
CPT Jay Bucci MC (Resident, Internal Medicine Service)  
CPT(P) Donald Helman MC (Fellow, Pulmonary & Critical Care Medicine Service)

## II. LIST OF PROTOCOLS BY DEPARTMENT AND SERVICE

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<b><i>Aberdeen Proving Ground</i></b>		
01-86001	Walsworth, Matthew, CPT SP. Efficacy of Stretching and Mobilization with Neutral Wrist Splinting Versus Neutral Wrist Splinting Alone in Patients with Carpal Tunnel Syndrome: A Randomized Trial. (1/16/2001)	458
02-86002	Knapik, Joseph, PhD DAC. Injury Control and Running Footwear. (3/12/2002)	655
<b><i>CHPPM</i></b>		
02-98001E	Piotrowski, Mark, MAJ DE. USACHPPM Dental Mouthguard Study. (12/19/2001)	Exempt
<b><i>DENTAC</i></b>		
02-94000E	Trebus, Daniel M., MAJ DE. Prevalence of Soft Tissue Injuries with Use of Commercial Endotracheal Tube Holders. (9/25/2002)	Exempt
02-94001	Trebus, Daniel M., MAJ DE. The Effect of Platelet Rich Plasma on Postoperative Pain, Edema, and Ecchymosis in Cervicofacial Rhytidectomy: A Pilot Study. (1/15/2002)	679
<b><i>Department of Allergy-Immunology</i></b>		
01-33001	Kim, Theodore, MAJ MC. In Vitro Gamma-Interferon Response to MTB Antigens in BCG-Vaccinated Individuals and Those with Equivocal PPD Skin Test Compared to Negative and Positive Control Subjects. (2/13/2001)	406
01-33002	Waibel, Kirk H., CPT MC. Suppression of Ragweed Wheal Response by Montelukast: A Double-blind Study. (3/20/2001)	407
02-33003	Katial, Rohit, MAJ MC. Comparing the Rate of Return of the Wheal-and-Flare Responses in Skin Prick Testing to Both Histamine Control and Aeroallergens after Discontinuing Two Weeks of Therapeutic Daily Dose Fexofendadine. (2/26/2002)	592
02-33005E	Martin, Bryan L., LTC MC. Vaccine Temp Associated Adverse Events: Review of Clinical Cases Referred To A Tertiary Medical Center. (12/19/2001)	Exempt
02-33006E	Nelson, Michael R., LTC MC. The role of skin testing and RAST in the evaluation of bee sting allergy. (1/30/2002)	Exempt
03-33004	Klote, Mary M., MAJ MC. Oropharyngeal Vaccinia Virus Presence After Smallpox Vaccination. (12/3/2002)	790
03-33005	Nelson, Michael R., LTC MC. Immune Responses to Smallpox Vaccination. (12/10/2002)	791
03-33006	Klote, Mary M., MAJ MC. Cell Mediated Immune Response to Anthrax Vaccination. (5/20/2003)	792
03-33007	Carr, Warner W., MAJ MC. A Comparison of Skin Test Devices for Prick Testing. (8/26/2003)	793

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03-33007EX	Carr, Warner W., MAJ MC. Epinephrine Prescribing patterns for Anaphylaxis at WRAMC. (12/16/2002)	Exempt
03-33008EX	Carr, Warner W., MAJ MC. Use of HE2000 in the Treatment of Leishmaniasis in the U937 Cell Line. (1/3/2003)	Exempt
03-33009EX	Mikita, Cecilia, CPT MC. Cutaneous Manifestations After Smallpox Vaccination. (2/20/2003)	Exempt
03-33010EX	Kim, Theodore, MAJ MC. Smallpox Vaccination Site Reactions in Primary and Re-Vaccination Candidates. (2/20/2003)	Exempt
03-33011EX	Klote, Mary M., MAJ MC. Trends in Allergy Immunotherapy Prescribing: A Decade in Review. (6/17/2003)	Exempt
03-33012EX	Song, Ted Taiil, CPT MC. Gender differences in subcutaneous fat: Do we need gender based epinephrine needle?. (8/1/2003)	Exempt
3369	Kosisky, Susan, DAC. Survey of Prevalent Pollen and Fungal Aeroallergens in the Washington DC Area. (5/11/1993)	141
3372	Engler, Renata J.M., COL MC. Mosquito Hypersensitivity: Immunology and Value of Skin Testing with Whole Body Mosquito Extracts. (12/21/1993)	143
3385	Engler, Renata J.M., COL MC. Adverse Reactions with Intravenous Immunoglobulin Therapy. (12/10/1996)	144
3390-99	Nelson, Michael R., LTC MC. A Phase 3 Study to Determine the Efficacy and Safety of C1-Inhibitor (HUMAN) Vapor Heated, Immuno in Subjects with Hereditary Angioedema (HAE). (5/25/1999)	145

### ***Department of Clinical Investigation***

00-9202AD	Sjogren, Maria H., COL MC. Efficacy of Therapy with Interferon (interferon alfa-2b or Pegylated Interferon alfa-2b) in Combination with Ribavirin for Chronic Hepatitis C Infections in Egypt. (1/27/2000)	Admin
01-92002	Sjogren, Maria H., COL MC. A Prospective, Randomized, Multicenter, Open-Label, Comparative Safety Study of Pegasy® vs. Pegasys® Plus Ribavirin Treatment vs. A Twelve-Week Treatment Delay in Patients with Chronic Hepatitis C. (1/23/2001)	463-468
01-92003	Sjogren, Maria H., COL MC. Hepatitis C Virus Infection: Mechanism of Disease Progression. (2/20/2001)	469
01-92004	Rojkind, Marcos, MD DAC. Interleukin-6 and Tumor Necrosis Factor-Alpha Role In Alcoholic Liver Cirrhosis. (9/11/2001)	472
01-92005	Rojkind, Marcos, MD DAC. The Role of the Acute Phase Response in Alcoholic Liver Cirrhosis. (9/14/2001)	473
01-92006	Rojkind, Marcos, MD DAC. Alcohol-Induced Liver Fibrosis: An In Vitro Model. (9/14/2001)	474
01-9201	Bednarek, Jana, PhD DAC. Hepatitis G Virus and Aplastic Anemia. (12/5/2000)	461

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02-92007	Sjogren, Maria H., COL MC. A Multicenter Double-Blinded Study in Patients with Compensated Cirrhosis Due to Chronic Hepatitis C Who are Non-Responders to Prior Interferon Alfa or Interferon Alfa + Ribavirin Therapy, Comparing Treatment with Thymosin Alpha 1 + Peginterferon Alfa-2a With Peginterferon Alfa-2a + Placebo. (10/23/2001)	670
02-92007E	Fileta, Bader, DAC. Analysis of Malaria Recombinant Protein Vaccines. (10/2/2001)	Exempt
02-92008	Sjogren, Maria H., COL MC. A Phase II, Double-Blind, Randomized, Placebo-Controlled, Multicenter Study of the Safety and Anti-Fibrotic Efficacy of Interferon Gamma-1b (IFN-y 1b) in Patients with Severe Liver Fibrosis or Compensated Cirrhosis Due to Hepatitis C. (11/20/2001)	672
02-92009	Sjogren, Maria H., COL MC. A Multicenter Double-Blinded Study in Non-Cirrhotic Patients with Chronic Hepatitis C Who Are Non-Responders to Prior Interferon Alfa or Interferon Alfa + Peginterferon Alfa-2a with Peginterferon Alfa-2a + Placebo. (3/26/2002)	673
02-92010	Sjogren, Maria H., COL MC. A Phase II Open label Study to Evaluate the Safety and Efficacy of RU-8811, in Patients with Types 3 or 4 Non-Alcoholic Fatty Liver Disease (NAFL). (4/23/2002)	676
02-92012	Sjogren, Maria H., COL MC. Combination of Ribavirin with Interferon Alfacon-1 or with Pegylated Interferon Alfa 2b as Initial Treatment for Difficult to Treat Subjects Chronically Infected with Hepatitis C Virus - Genotype 1. (6/25/2002)	678
03-92008EX	Marin, Raul, LTC MC. Effectiveness of Research Education. (2/20/2003)	Exempt
03-92009EX	Rojkind, Marcos, MD DAC. The role of the acute phase cytokines on the formation of functional gap junctions in hepatic stellate cells: A flow cytometric analysis. (6/25/2003)	Exempt
03-92010EX	Rojkind, Marcos, MD DAC. Characterization of proteins differentially expressed in acetaldehyde-treated hepatic stellate cells. (6/25/2003)	Exempt
03-92011EX	Rojkind, Marcos, MD DAC. The role of G10 maternal RNA in acetaldehyde-mediated fibrogenesis in vitro. (6/25/2003)	Exempt
03-92013	Sjogren, Maria H., COL MC. Management of Anemia and Neutropenia Associated with Pegylated Interferon + Ribavirin Treatment of Chronic Hepatitis C: An Open-Label Dose Titration Study of Darbepoetin Alfa and Filgrastim (Amendments 1, 2, 3, 4, & 5). (2/11/2003)	826
03-92014	Rojkind, Marcos, MD DAC. A Functional Co-culture of Hepatocytes and Hepatic Stellate Cells. (8/5/2003)	827
03-92015	Zhou, Yaling, PhD DAC. Evaluation of Dendritic Cell Functions During Hepatitis C Virus Infection and IFNa/Ribavirin Therapy. (9/23/2003)	828
9206	Yuan, Christina M., COL MC. Are Heat Shock Proteins Target Antigens of the Immune System in Renal Allograft Recipients?. (4/9/1996)	223
9221-99	Sjogren, Maria H., COL MC. Combination of Ribavirin with Interferon Alfacon-1 or With Interferon Alfa 2b as Initial Treatment for Chronic Hepatitis C. (12/15/1998)	224



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9223-99	Burch, Henry B., LTC MC. An Investigation of Oxidative Damage to Proteins in Thyroid Autoimmunity. (4/6/1999)	227
<b><i>Department of Medicine</i></b>		
03-19012EX	Fishbain, Joel, LTC MC. The epidemiology and clinical impact of Acinetobacter baumannii infections in soldiers returning from Operation Enduring Freedom and Operation Iraqi Freedom. (9/29/2003)	Exempt
<b><i>Cardiology Service</i></b>		
00-1201	Taylor, Allen J., LTC MC. ARBITER: Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol - A Randomized Trial Comparing the Effects of Atorvastatin and Pravastatin on Carotid Intima-Media Thickness. (10/26/1999)	230
01-12001	Taylor, Allen J., LTC MC. Acetylsteyne for the Prevention of Contrast Associated Nephropathy in Diabetic Patients Undergoing Coronary Angiography. (1/23/2001)	313
01-12002	Malik, Anwar K., MAJ MC. Remote Echocardiographic Consults - Diagnostic Concordance - Intra and Inter Consults. (6/5/2001)	316
01-12003	Taylor, Allen J., LTC MC. ARBITER II: Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol - A Randomized, Placebo-controlled, Double-Blind Study. (7/31/2001)	317
02-12004	Taylor, Allen J., LTC MC. The Effects of Simvastatin on Heart Rate Variability in Dilated Cardiomyopathy. (10/16/2001)	480
02-12005	Wiley, Thomas A., LTC MC. Ventricular Resynchronization Therapy Randomized Trial (VecToR). (11/29/2001)	481
02-12006NR	Simpson, Daniel, MAJ MC. Review of a Humanitarian Device Document. (3/26/2002)	482
02-12007	Isenbarger, Daniel W., MAJ MC. Utility of the Pace-ECG for Diagnosis of Cardiac Hypertrophy. (8/20/2002)	483
02-12008	Sullenberger, Lance, CPT MC. The Accuracy of Physical Examination for the Diagnosis of Aortic Valvular Sclerosis. (8/27/2002)	484
03-12003EX	Taylor, Allen J., LTC MC. Pharmacologic interactions with simvastatin in the National Capital Area Military Medical Treatment Facilities: Their frequency and the appropriateness of laboratory monitoring. (10/18/2002)	Exempt
03-12004EX	Kent, Steven M, MAJ MC. Prevalence of positive findings for endocarditis on transesophageal echocardiography when performed as a result of S. aureus bacteremia. (6/4/2003)	Exempt
03-12009	Taylor, Allen J., LTC MC. ARBITER III: Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol - A 1-year Open Label Investigation on the Effects of Long-Acting Niacin on Carotid Intimal Thickness. (12/10/2002)	685
03-12010	Dixon, William C. IV, MAJ MC. Pride Study: Protection During Saphenous Vein Graft Intervention to Prevent Distal Embolization. (12/17/2002)	686

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03-12012	Welka, Stephen, MAJ MC. Organized Program to Initiate Life-Saving TreatMent in HospitaliZed Patients with Heart Failure (OPTIMIZE-HF): An Internet-Based REGISTRY AND Process of Care Improvement Program for Heart Failure Patients. (2/4/2003)	688
03-12013	Simpson, Daniel, MAJ MC. A Prospective United States Investigation of the CARDIA STAR Patent Foramen Ovale Closure Device. (3/25/2003)	689
03-12014	Welka, Stephen, MAJ MC. Warfarin Versus Aspirin in Reduced Cardiac Ejection Fraction (WARCEF). (4/8/2003)	690
03-12015	Simpson, Daniel, MAJ MC. Protocol XRP4563B/4001: A Prospective, Open-Label, Randomized, Parallel-Group Investigation to Evaluate the Efficacy and Safety to Enoxaparin Versus Unfractionated Heparin in Subjects Who Present to the Emergency Department with Acute Coronary Syndrome. (7/15/2003)	691
03-12016	Lee, Joseph Y., MAJ MC. Pulsus Paradoxus in Central Obesity. (8/26/2003)	692
1215	Taylor, Allen J., LTC MC. The Utility of Electron Beam Computed Tomography (EBCT) as a Screening Test for Coronary Artery Disease, and as an Intervention for Risk Factor Modification Among Over 40 Active Duty Personnel. (11/25/1997)	8
1218-98	Calagan, Jennifer L., LTC MC. Assessment of Clinical Outcome Using Prothrombin Time Patient Self Testing (PST) to Monitor Long Term Anticoagulation Therapy. (6/16/1998)	9
1224-99	Vernalis, Marina, COL MC. Non-Invasive Coronary Artery Disease Reversal. (9/21/1999)	11
<b><i>Dermatology Service</i></b>		
03-18000EX	Meyerle, Jon, CPT MC. An Outbreak of Urticaria Among Soldiers Deploying for Combat. (3/24/2003)	Exempt
03-18001	Norton, Scott A., LTC MC. Palatability Comparison of Children's Corticosteroid Suspensions: A Randomized Double-Blind Trial. (10/8/2002)	724
<b><i>Endocrine Service</i></b>		
00-1303	Bernet, Victor J., LTC MC. Galectin-3 Levels as a Marker of Thyroid Cancer in Fine-Needle Aspiration (FNA) Samples. (2/8/2000)	231
01-13001	Stocker, Derek J., MAJ MC. A Comparison of the Effects of Rosiglitazone and Metformin on Markers of Inflammation and Carotid Plaque Burden in Patients with Type 2 Diabetes Mellitus. Cardiovascular Effects of Hypoglycemic Medications in Diabetes - CHD Study. (1/23/2001)	318
01-13002	Vigersky, Robert A., COL MC. Using Telemedicine and Wireless Technology to Improve Diabetic Outcomes in Poorly Controlled Patients. (3/20/2001)	319
01-13003	Vigersky, Robert A., COL MC. The Avandia Worldwide Awareness Registry (AWARE): Comparison of Avandia and Actos in "Real World" Medical Practice. (3/27/2001)	322

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01-13005	Langely, Roy W., MAJ MC. Determination of Thyroid Nodule Malignancy with 18F-FDG Coincidence Imaging and Tc-99m Depreotide Scintigraphy. (6/19/2001)	324
02-13006	Vaishnav, Yashesh N., PhD DAC. Investigations on Y-Ray-Induced Alterations in Gene Expression Profiles in pRC-CMV and Ret/PTC-3 Oncogene Expressing FRTL-5 Thyroid Cell Lines Utilizing cDNA Expression Array. (11/13/2001)	485
02-13007	Vigersky, Robert A., COL MC. The Use of Heart Rate Variation to Determine the Prevalence and Prognostic Significance of Autonomic Neuropathy in Patients with Either Diabetes Mellitus or Cardiovascular Disease. (2/26/2002)	487
02-13008	Harner, Kyle C., CPT MC. Effect of A Single Intra-Articular Steroid Injection on Serum Glucose Levels in Patients with Type 2 Diabetes Mellitus. (3/12/2002)	489
02-13009	Vigersky, Robert A., COL MC. An Assessment of Ocular Lens Fluorescence Measurements for the Detection of Diabetes: A Joint Joslin Diabetes Center, Tripler Army Medical Center and Walter Reed Army Medical Center Study. (4/23/2002)	490
02-13009E	Burch, Henry B., LTC MC. Comparison of Total Hyperthyroid Time in Patients Previously Pre-treated or Not-pre-treated with Antithyroid Drugs Before Ablation With Radioiodine for Graves' Disease: A Retrospective Analysis. (1/30/2002)	Exempt
02-13010	Glistner, Babette C., CPT MC. Home Fructosamine Testing as a Cost-Effective Adjunctive Tool for Improving Glucose Control in Inadequately Controlled Type 2 Diabetes Mellitus. (5/28/2002)	491
02-13010EX	Vigersky, Robert A., COL MC. The Sensitivity and Specificity of Stereoscopic Non-Mydriatic Digital Retinal Photography in Detecting Diabetic Retinopathy. (9/30/2002)	Exempt
02-13011	Wallace, Eugene, CPT MC. The Effects of Variations in Diet Composition on Body Mass. (8/6/2002)	492
02-13012	Vigersky, Robert A., COL MC. Continuous Glucose Monitoring in Patients with Type 2 Diabetes Mellitus. (9/17/2002)	494
03-13012EX	Wallace, Eugene, CPT MC. Papillary Thyroid Cancer: A Review of the Walter Reed Experience. (2/20/2003)	Exempt
03-13013	Vaishnav, Yashesh N., PhD DAC. Quantitative Assessment of Cyclooxygenase-2 Gene/Mrna Expressions in Paraffin Embedded Benign and Cancerous Thyroid Tissues. (4/15/2003)	693
03-13014	Vigersky, Robert A., COL MC. A One-Year, Open, Randomized, Parallel, Three-Arm Study, Comparing Exubera® (Insulin Dry Powder Pulmonary Inhaler) Vs. Avandia® (rosiglitazone Maleate) as Add-on Therapy vs. Exubera® Substitution of Sulfonylurea in Patients with Type 2 Diabetes, Poorly Controlled on Combination Sulfonylurea and Metformin Treatment. (6/10/2003)	694
03-13015	Robbins, Iris, BA DAC. Evaluation of Somatostatin Receptor (SSTR) Response to rh TSH in Various Thyroid Cancer Cell Lines. (8/5/2003)	695

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00-1404	Cumings, Mark D., MAJ MC. A Comparison of Pediatric and Adult Colonoscopes in Adult Patients Presenting for Routine Colonoscopy. (3/21/2000)	235
00-1407	Hwang, Inku, MAJ MC. Tele-Hepatitis Phase I: Validation of desktop Video Teleconferencing (VTC) System at 384 kb ISDN for Evaluation of Patients with Hepatitis. (5/16/2000)	236
00-1408	Holtzmuller, Kent, COL MC. A Randomized Multicenter Trial Comparing Induction PEG Intron-A Plus Ribavirin Versus PEG Intron-A Plus Ribavirin in Patients...Not Responded or Have Relapsed..Based Therapy for Chronic Hepatitis C, With Maintenance ... Who Continue to Remain Non-Responsive. (7/18/2000)	237
01-14001	Duncan, Marten, CPT MC. Association of Helicobacter pylori Infection with Coronary Heart Disease Detected by Electron Beam CT. (1/9/2001)	325
01-14002	Baroni, Darren S., MAJ MC. An Efficacy and Safety Study of Intravenous Pantoprazole in the Prevention of Recurrent Peptic Ulcer Bleeding After Successful Hemostasis (Sponsored Study by Wyeth-Ayerst Research). (4/17/2001)	326
01-14003	Napierkowski, John, MAJ MC. Effect of Complete Intraesophageal Acid Ablation Upon Cellular Markers of Proliferation, Differentiation, and Apoptosis in Long-Segment Barrett's Esophagus. (4/24/2001)	327
01-14004	Holtzmuller, Kent, COL MC. The Timing of Liver Enzyme Elevation and Hepatitis C Seroconversion in a Cohort of United States Military Gulf War Veterans. (5/1/2001)	328
01-14005	Holtzmuller, Kent, COL MC. Tele-Hepatitis Phase I: Validation of Desktop Video Teleconferencing for Evaluation of Patients with Hepatitis C. (5/29/2001)	329
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02-14007	Mulhall, Brian P., MAJ MC. The Role of Gastroesophageal Reflux Disease (GERD) in Upper Airway Reactivity Syndrome (UARS). (10/16/2001)	495
02-14007E	Hwang, Inku, MAJ MC. InVivo Localization of Glandular Dysplasia in the Esophagus: Identification of Differentially Expressed Molecules in Dysplastic Barrett's Esophagus Using Archived Tissue. (10/26/2001)	Exempt
02-14008	Mulhall, Brian P., MAJ MC. The Effect of Interferon Therapy on Hearing in Adult Patients with Chronic Hepatitis C. (10/16/2001)	497

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02-14009	Mulhall, Brian P., MAJ MC. The Clinical Impact of Gastroesophageal Reflux in Adult Patients with Obstructive Sleep Apnea. (3/26/2002)	499
02-14009E	Cumings, Mark D., MAJ MC. The Significance of Belching in Upright Reflux Disease. (3/20/2002)	Exempt
02-14010	Wong, Roy K.H., COL MC. A Multicenter, Double-Blind, Three-way Crossover Intraesophageal and Intragastric pH Study of Three Esomeprazole Treatment Regimens in Documented Barrett's Esophagus Patients. (3/26/2002)	501
02-14010E	Cumings, Mark D., MAJ MC. The Significance of Postprandial Reflux in Upright Reflux Disease. (3/20/2002)	Exempt
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02-14011E	Hwang, Inku, MAJ MC. Cytokeratin 7/20 Staining Patterns and Cellular Proliferation in Long-Segment Barrett Esophagus (LSBE), Short-Segment Barrett Esophagus (SSBE), and Endoscopically Normal Esophagogastric Junction with Specialized Intestinal Metaplasia (EGJ-SIM). (3/20/2002)	Exempt
02-14012	Duncan, Marten, CPT MC. Use of a Hyperspectral Imaging System for Dysplasia Screening in Patients with Long Segment Barrett's Esophagus - A Pilot Study. (5/28/2002)	503
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02-14013	Duncan, Marten, CPT MC. Twenty-Four Hour pH Monitoring and Histologic Evaluation in Patients with Tongues in the Distal Esophagus: Are These Findings Clinically Relevant?. (9/17/2002)	504
03-14013EX	Friend, Julia, DAC. Treatment outcomes in hepatitis C: the impact of dose adjustments secondary to complications. (10/25/2002)	Exempt
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Collura-Burke, C, B Speller-Brown, LJ Smith, MR Nelson, HJ Schmidt : Asthma education and its effect on quality of life. Annual Meeting of the Association of Uniformed Allergists & Immunologists, Denver CO, 2003 March.	Presentation
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Enger, RJM : Immunization. Immune-Based Therapies, Allergy & Immunology Medical Knowledge Self-Assessment Program, 3rd edition, American Academy of Allergy, Asthma, and Immunology, 5:, 2003.	Publication
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Engler, RJ : Adverse reactions to alternative medication. World Allergy Organization, Vancouver BC Canada, 2003 September.	Presentation
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Engler, RJ : Screening for Other Important Risk Factors. DOD Smallpox Preparedness Conference, Crystal City VA, 2002 October-November.	Presentation
Engler, RJ : Smallpox Vaccine - From Medical Exemptions to Adverse Events - New Challenges for the Allergist-Immunologist. 5th Annual Allergy for the Allergist Meeting, San Antonio TX, 2003 April.	Presentation
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Engler, RJ : Vaccinations in support of Homeland Defense. West TX Homeland Defense Symposium, Dyess AFB 7th Medical Group, Dyess AFB TX, 2003 April.	Presentation
Engler, RJM : Alternative and Complementary Therapy for Allergic Disease. Allergy and Clinical Immunology, Medical Knowledge Self-Assessment Program, 3rd edition, American Academy of Allergy, Asthma, and Immunology, 4:, 2003.	Publication
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Katial, RK : Diagnostic Laboratory Immunology. Allergy & Immunology Medical Knowledge Self-Assessment Program, 3rd edition, American Academy of Allergy, Asthma, and Immunology, 7:, 2003.	Publication
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Martin, BL : An overview of multi-media - manipulating an image. Workshop on "A primer on how to make multi-media presentations", Annual Meeting of the American Academy of Allergy, Asthma, and Immunology, Denver CO, 2003 March.	Presentation
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Mikita, CP, SA Norton, MR Nelson, RJ Engler : Cutaneous reactions after smallpox vaccinations. 2003 Military Allergy Program, 17th Annual Harold S. Nelson Allergy-Immunology Symposium, 2003 March.	Abstract
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Nelson, MR : The Walter Reed smallpox immunization program. Hackensack University Medical Center, Hackensack NJ, 2003 April.	Presentation
Smith, LJ : Hot topics in pediatric allergy, asthma and immunology - Year-in-Review Session. Annual Meeting of the American Academy of Allergy, Asthma, and Immunology, Denver CO, 2003 March.	Presentation
Yacovone, MA, P Powers, R Katial : Primary autoimmune neutropenia associated with endocrinopathy. J Allergy Clin Immunology, 111(3):S318 (abstract 999), 2003 February.	Abstract

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Marin, R, S Davis, C Christ, J Choi, R Howard, R Henderson, J Keais, C Quick : Neuromuscular rehabilitation via telebiofeedback as a portal for home care. Telemed J E-Health, 9(Suppl1):S-77, 2003.	Abstract
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Sjogren, M : Immunization and the decline of viral hepatitis as a cause of acute liver failure. Hepatology, 38(3):554-556, 2003 September.	Publication
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Abbott, KC, FC Trespacios, AJ Taylor, LY Agodoa : Atrial fibrillation in chronic dialysis patients in the United States: risk factors for hospitalization and mortality. BMC Nephrology, 4(1):1, 2003 January.	Publication
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Bautista, L, AJ Taylor, JE Atwood, PG O'Malley : Association between C-reactive protein and hypertension among low cardiovascular risk subjects. Circulation, 107(7):7001e, 2003.	Abstract
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Cho, S, JE Atwood : Peripheral Edema. Am J Med, 113(7):580-586, 2002 November.	Publication
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Creel, NB, GW Turiansky : Cutaneous sarcoidosis in herpes zoster scars. The Gross and Microscopic Dermatology Symposium, American Academy of Dermatology Meeting, San Francisco CA, 2003 March.	Presentation
Darling, TN : Allelic deletion of the TSC2 gene in tuberous sclerosis skin tumors and cultured stromal cells. Doris Duke Charitable Foundation Clinical Scientist Meeting, Newport RI, 2002 November-December.	Presentation
Darling, TN : Hyperphosphorylation of P70S6K and ribosomal protein S6 in tuberous sclerosis skin tumors is inhibited by rapamycin. USMCI 3rd Annual Scientific Colloquium, 2003 September.	Presentation
Darling, TN : Oncogenes and Tumor Suppressor Genes in Disease. American Academy of Dermatology, San Francisco CA, 2003 March.	Presentation
Darling, TN : Skin care for children and adults with proteus syndrome. Proteus Syndrome Foundation Conference, Workshop Leader, NIH, Bethesda MD, 2002 October.	Presentation

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Dolan, CK, MA Hall, GW Turiansky : Secondary erythralgia in an HIV-1positive patient. AIDS Reader, 13:91-93, 2003.	Publication
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Maggio, KL : Evaluation of Apligraf conditioned media topical preparation (Revitix) in laser resurfacing. Scripps Clinic, La Jolla CA, 2002-2003.	Presentation
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Maggio, KL : Skin Flaps Laboratory Session. Superficial Anatomy and Cutaneous Surgery Clinical Conference, La Jolla CA, 2003 July.	Presentation
Maino, KL, GW Turiansky : Porphyria cutanea tarda in end stage renal failure. The Gross and Microscopic Dermatology Symposium, American Academy of Dermatology Meeting, San Francisco CA, 2003 March.	Presentation
Meyerle, J : Superficial acral fibromyxoma of the index finger. Southern Medical Association Conference, 2002 November.	Presentation
Meyerle, JH, GW Turiansky : Cytomegalovirus infection involving a chronic perianal ulcer in a patient with AIDS. The Gross and Microscopic Dermatology Symposium, American Academy of Dermatology Meeting, San Francisco CA, 2003 March.	Presentation
Murphy, ME, GW Turiansky : Onchocerciasis in a traveler to Cameroon. The Gross and Microscopic Dermatology Symposium, American Academy of Dermatology Meeting, San Francisco CA, 2003 March.	Presentation
Murphy, ME, J Boyer, J Zitelli : The surgical management of the Spitz Nevus. American College of Mohs Micrographic Surgery and Oncology, American Society of Dermatologic Surgery National Meeting, Chicago IL, 2002 October.	Presentation
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Norton, SA : Skin signs of political violence. Colorado Dermatology Society Annual Meeting, Denver CO, 2002 October.	Presentation
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Schwartz, J, SA Norton : Useful plants of dermatology - VI The may apple (Podophyllum). J Am Acad Dermatol, 47:774-775, 2002 November.	Publication
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Smalling, CR, GW Turiansky : Segmental neurofibromatosis - Type I. The Gross and Microscopic Dermatology Symposium, American Academy of Dermatology Meeting, San Francisco CA, 2003 March.	Presentation
Sperling, LC : Dermatology A-Z. USU Family Practice Review Course, A Capital Conference, 2003 June.	Presentation
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Turiansky, GW : Common dermatological conditions of the face and hands (Part II). Rader Health Clinic, Fort Myers VA, 2003 February.	Presentation
Turiansky, GW : Cutaneous manifestations of HIV-1 infection before and after the advent of HAART. American Academy of Dermatology Summer ACADEMY 2003 Meeting, Focus Session, Hyatt Regency, Chicago IL, 2003 July.	Presentation
Turiansky, GW : Dermatoses in HIV-1 Disease. US-Ukraine HIV/AIDS 2002 International web-based UDL Program, 2002 December.	Presentation
Vogel, J, C Yee, TN Darling : Application of molecular biology to the study of skin. Dermatology (Bologna, Jorizzso, and Rapini, eds) 1st ed, Harcourt Health Sciences, London, 2003.	Publication
Willard, RJ, MJD Auerbach : Targetoid hemosiderotic hemangioma. The Gross and Microscopic Dermatology Symposium, American Academy of Dermatology Meeting, San Francisco CA, 2003 March.	Presentation
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Abbott, KC, VJ Bernet, LY Agodoa, CM Yuan : Diabetic ketoacidosis and hyperglycemic hyperosmolar syndrome after renal transplantation in the United States. BMC Endocr Disord, 3(1):1, 2003 March.	Publication
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Bernet, VJ, J Anderson, Y Vaishnav, B Solomon, CF Adair, M Saji, KD Burman, HB Burch, MD Ringel : Determination of galectin-3 messenger ribonucleic acid overexpression in papillary thyroid cancer by quantitative reverse transcription-polymerase chain reaction (RT-PCR). J Clin Endocrinol Metab, 87(10):4792-4796, 2002 October.	Publication
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Bursell, S, P Conlin, M Horton, R Vigersky, A Cavallerano, LM Aiello : The Joslin Vision Network picture archiving and communication system (PACS) for eye health care. Diabetes Technology Society Annual Meeting, 2002 October.	Presentation

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Langley, R, R Bridwell, J Montilla, C Shriver, VJ Bernet : 99mTc-Depreotide scintigraphy and 18 F-Fluorodeoxyglucose (FDG) PET for the localization of persistent metastatic papillary thyroid carcinoma - A case report. 75th Annual Meeting of the American Thyroid Association, 2003 September.	Abstract
McMahon, J, D Gaitonde, R Vigersky : Macroprolactinoma and severe hypogonadism - A case report. Army-American College of Physicians, Arlington VA, 2002 November.	Presentation
Ringel, MD, E Hardy, VJ Bernet, HB Burch, F Schuppert, KD Burman, M Saji : Metastin receptor is overexpressed in papillary thyroid cancer and activates MAP kinase and Akt in thyroid cancer cells. J Clin Endocrinol Metab, 87:2399-2402, 2002 October.	Publication
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Stocker, DJ : Management of the Bariatric Surgery Patient - Endocrinology and Metabolism Clinics of North America. Burch, H. (ed.), 32(2):437-457, 2003 June.	Publication
Stocker, DJ, AJ Taylor, RW Langley, RS Howard, RA Vigersky : Comparison of Rosiglitazone vs. Metformin on markers of coronary heart disease in patients with Type 2 Diabetes Mellitus. Diabetes Metab, 29(2):4S341-342, 2003 August.	Abstract
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Stocker, DJ, WF Kelly, TM Fitzpatrick, VJ Bernet, HB Burch : Bilateral external laryngoceles following radioactive iodine ablation for Graves' Disease. Archives Intern Med, 162(17):2007-2009, 2002 (FY03).	Publication
Vigersky, R : PC-SPES - An "Alternative" prostate cancer treatment causes adverse effects on thyroid hormone homeostasis. Endocrine Society Annual Meeting, Philadelphia PA, 2003 June.	Presentation
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Vigersky, RA, E Hanson, E McDonough, T Rapp, RS Galen : A wireless diabetes management and communication system. <i>Diabetes Technology Society Annual Meeting</i> , 2002 October.	Presentation
<b><u>Gastroenterology Service</u></b>	
Cash, BD : Functional dyspepsia. <i>Medscape Gastroenterol. Expert Column</i> , 2002 December.	Publication
Cash, BD : Update on PPIs. <i>Medscape Gastroenterol. Conference Summary</i> , 2002 November.	Publication
Cash, BD, PS Schoenfeld, AP Flood, DA Lieberman : Colorectal cancer screening in asymptomatic, average risk females: is age 50 the proper starting point? (poster). 67th Annual Meeting of the American College of Gastroenterology, Seattle WA, 2002 October.	Presentation
Cash, BD, PS Schoenfeld, D Rex : An evidence-based medicine approach to studies of diagnostic tests. <i>Clin Gastroenterol Hepatol</i> , 1:136-144, 2003.	Publication
Cash, BD, WD Chey : Diagnostic tests in irritable bowel syndrome patients. <i>Dig Health Matters</i> , 12:5-8, 2003 Spring.	Publication
Cossentino, MJ, C Maydonovitch, L Belle, RKH Wong : The effect of baclofen on patients with gastroesophageal reflux disease: a prospective, double-blind, placebo-controlled study. <i>Gastroenterology</i> , 124(4 Suppl 1):A-226, 2003.	Abstract
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deLorimer, AJ, W Byrd, ER Hall, WM Vaughn, D Tang, ZJ Roberts, CE McQueen, FJ Cassels : Murine antibody response to intranasally administered enterotoxigenic <i>Escherichia coli</i> colonization factor CS6. <i>Vaccine</i> , 21:2548-2555, 2003.	Publication
Dunaway, PM, JJ Napierkowski, CL Maydonovich, JL Lee, RK Vartanian, H Yang, LS Belle, RK Wong : Does acute acid exposure followed by normalization of intraesophageal pH affect surrogate markers in Barrett's epithelium?. <i>Dig Disease Week</i> , Orlando FL, 2003 May.	Presentation
Dunaway, PM, JJ Napierkowski, CL Maydonovich, JL Lee, RK Vartanian, H Yang, LS Belle, RK Wong : Does acute acid exposure followed by normalization of intraesophageal pH affect surrogate markers in Barrett's epithelium?. <i>Gastroenterology</i> , 124(4 Suppl 1):A-641, 2003.	Abstract
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Duncan, M, J Grossmann, A Zigler, H Moskovitz, C Maydonovitch, K Holtzmuller, RKH Wong : Hyperspectral imaging (HIS) - A new approach to identifying mucosal irregularities. Dig Disease Week, Orlando FL, 2003 May.	Abstract
Duncan, MB, MT Smith : An unusual case of colonic lymphoma presenting as a diminutive colon polyp. Army Regional ACP-ASIM Meeting, Crystal City, VA, 2002 November.	Presentation
Duncan, MB, MT Smith : An unusual case of colonic lymphoma presenting as a diminutive colon polyp (poster). 67th Annual Meeting of the American College of Gastroenterology, Seattle WA, 2002 October.	Presentation
Esmat, G, AM Abouzied, F Abdel-Aziz, MK Mohamed, M Adel-Hamid, MS ElRaziky, SA Ismail, KR Zalata, NN Mikhail, A Fix, T Strickland, MH Sjogren : Treatment with peg-interferon alfa-2b (PEG-IFN) plus ribavirin compared to interferon alfa-2b (IFN alfa-2b) plus ribavirin on subjects with chronic hepatitis C infected with genotype 4 (poster). 53rd Annual Liver Meeting of the American Association for the Study of Liver Disease, Boston MA, 2002 November.	Presentation
Frizzell, E, KC Holtzmuller, B Fileta, D Nicholson, M Lewin-Smith, E Ladich, L Rabin, C Specht, MH Sjogren, FG Mullick : The timing of Hepatitis C seroconversion in a cohort of United States Military Gulf War veterans (GWVS). Army Regional ACP-ASIM Meeting, Crystal City, VA, 2002 November.	Presentation
Happe, MR, JA Eastone, JW Kikendall, RKH Wong : An unusual cause of acute dysphagia and chest pain in a young healthy female. Army Regional ACP-ASIM Meeting, Crystal City, VA, 2002 November.	Presentation
Happe, MR, PA Woodworth : Meckel's diverticulum in an adult gastrointestinal bleed. Am J Surg, 186(2):132-133, 2003 August.	Publication
Holtzmuller, KC : Approach to the liver mass. GI Grand Rounds, University of Texas at San Antonio, San Antonio TX, 2003 February.	Presentation
Holtzmuller, KC : Diagnosing liver masses in the 21st century. Walter Reed Gastroenterology Symposium, Tyson's Corner VA, 2003 March.	Presentation
Holtzmuller, KC : Hepatitis Update. Fort Bragg NC, 2003 February.	Presentation
Holtzmuller, KC : Hepatitis Update. DDEAMC Grand Rounds, 2002 Fall.	Presentation
Holtzmuller, KC : Hepatitis Update 2003. 12th Annual Capital Conference - A Family Practice Board Review, Andrews AFB MD, 2003 June.	Presentation
Holtzmuller, KC : Liver - Board Type Questions. William M. Steinberg's Board Review in Gastroenterology, Alexandria VA, 2002 October.	Presentation
Holtzmuller, KC, E Frizzell, B Fileta, et al : The timing of hepatitis C seroconversion in a cohort of US military Gulf War veterans. Hepatology, 36:553A, 2002 (FY03).	Abstract
Hwang, I, J-HR Choi, PJ Pickhardt, JH Smith, JA Butler, RKH Wong : Virtual colonoscopy - A multicentered screening study of military beneficiaries (poster). 67th Annual Meeting of the American College of Gastroenterology, Seattle WA, 2002 October.	Presentation
Hwang, I, JR Choi, PJ Pickhardt, JH Smith, JA Butler, WR Schindler, RKH Wong : Virtual colonoscopy - A multicentered screening study of military beneficiaries. 67th Annual Meeting of the American College of Gastroenterology, Seattle WA, 2002 October.	Presentation
Hwang, I, TB Calvit, BD Cash, KC Holtzmuller : Bell's palsy - A rare complication of interferon therapy for Hepatitis C (poster). 67th Annual Meeting of the American College of Gastroenterology, Seattle WA, 2002 October.	Presentation

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CITATION	TYPE
Hwang, I, TR Boal, SD Kennedy, RK Poropatich, KC Holtzmuller : Telehepatitis: validation of desktop videoteleconferencing (VTC) system at 384 kb connectivity for the evaluation of patients with chronic liver disease. <i>Gastroenterology</i> , 124(4 Suppl 1):A-556, 2003.	Abstract
Hwang, I, TR Boal, SD Kennedy, RK Poropatich, KC Holtzmuller : Telehepatitis: validation of desktop videoteleconferencing (VTC) system at 384 kb connectivity for the evaluation of patients with chronic liver disease. <i>Dig Disease Week</i> , Orlando FL, 2003 May.	Presentation
Jensen, D, et al : Demographics, risk factors, and outcomes of peptic ulcer hemorrhage in the US - Results of a large multicenter study. <i>DDW</i> , 03:101908, FY not submitted.	Abstract
Jensen, D, et al : Incidence of erosive esophagitis in a long-term study of patients with h. pylori eradication for ulcer hemorrhage. <i>DDW</i> , 03:101828, FY not submitted.	Abstract
Jensen, D, et al : Prevention of ulcer hemorrhage by h. pylori eradication. <i>DDW</i> , 03:101837, FY not submitted.	Abstract
Jensen, DM, T Savides, M Sitzler, H Frankl, K Esrason, S Hamamah, A Lee, Faigel, S Ho, R Wong, et al : Prevention of ulcer hemorrhage by H. pylori eradication. <i>Gastroenterology</i> , 124(4 Suppl 1):A-16, 2003.	Abstract
Jensen, DM, T Savides, M Sitzler, H Frankl, K Esrason, S Hamamah, A Lee, D Faigel, S Ho, R Wong, et al : Demographics, risk factors, and outcomes of peptic ulcer hemorrhage in the United States - Results of a large multicenter study. <i>Gastroenterology</i> , 124(4 Suppl 1):A-17, 2003.	Abstract
Jensen, DM, T Savides, M Sitzler, H Frankl, K Esrason, S Hamamah, A Lee, D Faigel, S Ho, R Wong, et al : Incidence of erosive esophagitis in a long-term study of patients with H. pylori eradication for ulcer hemorrhage. <i>Gastroenterology</i> , 124(4 Suppl 1):A-413, 2003.	Abstract
Jensen, DM, T Savides, M Sitzler, H Frankl, K Esrason, S Hamamah, A Lee, D Faigel, S Ho, R Wong, et al : Demographics, risk factors, and outcomes of peptic ulcer hemorrhage in the United States - Results of a large multicenter study. <i>Dig Disease Week</i> , Orlando FL, 2003 May.	Presentation
Jensen, DM, T Savides, M Sitzler, H Frankl, K Esrason, S Hamamah, A Lee, D Faigel, S Ho, R Wong, et al : Incidence of erosive esophagitis in a long-term study of patients with H. pylori eradication for ulcer hemorrhage. <i>Dig Disease Week</i> , Orlando FL, 2003 May.	Presentation
Jensen, DM, T Savides, M Sitzler, H Frankl, K Esrason, S Hamamah, A Lee, D Faigel, S Ho, R Wong, et al : Prevention of ulcer hemorrhage by H. pylori eradication. <i>Dig Disease Week</i> , Orlando FL, 2003 May.	Presentation
Katz, DE, AJ deLorimier, MK Wolf, ER Hall, FJ Cassels, JE vanHamont, RL Newcomer, MA Davachi, DN Taylor, CE McQueen : Oral immunization of adult volunteers with microencapsulated enterotoxigenic escheridia coli (ETEC) CS6 antigen. <i>Vaccine</i> , 21(5-6):341-346, 2003 January.	Publication
Lawitz, EJ, NS Bala, S Becker, G Brown, M Davis, R Dhar, KP Ganeshappa, S Gordon, K Holtzmuller, et al : Pegylated interferon alfa 2b and ribavirin for hepatitis C patients who were nonresponders to previous therapy (poster). <i>Dig Disease Week</i> , Orlando FL, <i>DDW American Gastroenterology Association</i> , 2003 May.	Presentation
Lee, JS, FM Moses : Endoscope disinfection and quality assurance practice patterns, <i>SGNA Daily Course Syllabus 3</i> . 30th Annual Course, <i>SGNA National Meeting</i> , Atlanta GA, 2003 May.	Abstract
Lee, JS, FM Moses : Current GI Endoscope Disinfection and Quality Assurance Practice Patterns (poster). 30th Annual Course, <i>SGNA National Meeting</i> , Atlanta GA, 2003 May.	Presentation
Matsumoto, C, SJ Swanson, LY Agodoa, KC Holtmuller, KC Abbott : Hospitalized gastrointestinal bleeding and procedures after renal transplantation in the United States. <i>J Nephrol</i> , 16(1):49-56, 2003 January-February.	Publication

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CITATION	TYPE
Moses, FM, J Lee : Surveillance cultures to monitor quality of gastrointestinal endoscope reprocessing. <i>Am J Gastroenterol</i> , 98(Jan):77-81, 2003.	Publication
Mulhall, BP, B Nelson, L Rogers, RK Wong : Herpetic esophagitis and intractable hiccups (singultus) in an immunocompetent patient. <i>Gastrointest Endosc</i> , 57(6):796-797, 2003 May.	Publication
Mulhall, BP, J Eastone, J Butler, P Schoenfeld : Incidence of advanced adenomas during early surveillance colonoscopy among patients with multiple or advanced adenomas at index colonoscopy. Army Regional ACP-ASIM Meeting, Crystal City, VA, 2002 November.	Presentation
Mulhall, BP, JP Ong, ZM Younossi : Non-alcoholic fatty liver disease: an overview. <i>J Gastroenterol Hepatol</i> , 17(11):1136-143, 2002 November.	Publication
Mulhall, BP, RK Wong : Infectious esophagitis. <i>Curr Treat Options Gastroenterol</i> , 6(1):55-70, 2003 February.	Publication
Mulhall, BP, RKJ Wong : Cost-effectiveness of screening for Barrett's esophagus in all patients presenting for upper endoscopy (poster). 67th Annual Meeting of the American College of Gastroenterology, Seattle WA, 2002 October.	Presentation
Napierkowski, J : Cytomegalovirus (CMV) infection presenting as a polypoid colonic mass. Army Regional ACP-ASIM Meeting, Crystal City, VA, 2002 November.	Presentation
Napierkowski, J, C Maydonovitch, L Belle, WT Brand Jr., K Holtzmuller : Wireless capsule endoscopy (WCE): a review of community gastroenterology experience. <i>Gastrointest Endosc</i> , 57(5):AB118 abstract S1527, 2003.	Abstract
Napierkowski, J, C Maydonovitch, L Belle, WT Brand Jr., K Holtzmuller : Wireless capsule endoscopy (WCE): a review of community gastroenterology experience. Dig Disease Week, Orlando FL, 2003 May.	Presentation
Napierkowski, J, RK Wong : Natalizumab - A new hope for Crohn's disease?. <i>Am J Gastroenterol</i> , 98(5):1197-1199, 2003 May.	Publication
Napierkowski, JJ, DS Sachar, M Cumings, K Kaplan, RK Wong : Image of the month - Cytomegalovirus (CMV) colitis. <i>Gastroenterology</i> , 125(1):8,281, 2003 July.	Publication
Napierkowski, JJ, DS Sachar, MD Cumings, RKH Wong : Cytomegalovirus (CMV) infection presenting as a polypoid colonic mass (poster). 67th Annual Meeting of the American College of Gastroenterology, Seattle WA, 2002 October.	Presentation
Pfeiffer, R, L McShane, M Wargovich, R Burt, W Kikendall, M Lawson, E Lanza, A Schatzkin : The effect of a low-fat, high fiber, fruit and vegetable intervention on rectal mucosal proliferation. <i>Cancer</i> , 98(6):1161-1168, 2003 September.	Publication
Sachar, DS, R Narayan, JW Song, HC Lee, TA Klein : Hantavirus infection in an active duty U.S. Army soldier stationed in Seoul Korea. <i>Mil Med</i> , 168(3):231-233, 2003 March.	Publication
Schoenfeld, P, J Shad, E Ormseth, W Coyle, B Cash, J Butler, W Schindler, WJ Kikendall, C Furlong, L Sobin, C Hobbs, D Cruess, D Rex : PREdictive value of Diminutive Colonic Adenoma Trial: THE PREDICT TRIAL. <i>Clin Gastroenterol Hepatol</i> , 1:195-201, 2003.	Publication
Sjogren, MH, KC Holtzmuller, M Smith, R Sjogren : Sustained antiviral response with consensus interferon (CIFN) plus ribavirin or interferon alfa-2b (IFN Alfa-2b) plus ribavirin in treatment-naive subjects with chronic hepatitis C - A pilot study. 53rd Annual Liver Meeting of the American Association for the Study of Liver Disease, Boston MA, 2002 November.	Presentation

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CITATION	TYPE
Tangrea, JA, PS Albert, E Lanza, K Woodson, D Corle, M Hasson, R Burt, B Caan, E Paskett, F Iber, JW Kikendall, P Lance, M Shike, J Weissfeld, A Schatzkin, Polyp Prevention Study Group : Nonsteroidal anti-inflammatory drug use is associated with reduction in recurrence of advanced and non-advanced colorectal adenomas. Cancer Causes Control, 14(5):403-411, 2003 June.	Publication
Torres, D, AH Andrews, C Maydonovich, RKH Wong : Utility of colonoscopy in the diagnosis and treatment of acute gastrointestinal hemorrhage admitted to the intensive care unit. Army Regional ACP-ASIM Meeting, Crystal City, VA, 2002 November.	Presentation
Unknown : Title not available. 8th Annual Young Investigator's Conference in Digestive Diseases, Phoenix AZ, 2003 April.	Presentation
Winters, GR III, CL Maydonovitch, RK Wong : Schatzki's rings do not protect against acid reflux and may decrease esophageal acid clearance. Dig Dis Sci, 48(2):299-302, 2003 February.	Publication
Wong, R : Non-GERD esophagitis - Infection, pill, or other causes. American College of Gastroenterology Post Graduate Course, Seattle WA, 2002 October.	Presentation
Wong, RKH : Abnormal LFTs. 38th Parallel Medical Society Meeting, U.S. Army Forces, Seoul Korea, 2003 April.	Presentation
Wong, RKH : Barrett's Esophagus. GI Grand Rounds, Cornell Medical School, New York NY, 2003 February.	Presentation
Wong, RKH : Barrett's Esophagus. GI Grand Rounds, Rush Presbyterian Medical Center, Chicago IL, 2003 February.	Presentation
Wong, RKH : Barrett's Esophagus. Grand Rounds, Howard University Medical School, Washington DC, 2003 April.	Presentation
Wong, RKH : Barrett's Esophagus - An overview. GERD 2003 Symposium, The Sacramento Veteran Administration Hospital in conjunction with The American College of Gastroenterology, 2003 June.	Presentation
Wong, RKH : Barrett's Esophagus - Concern's about screening and surveillance. Connecticut Medical Society, Hartford CT, 2002 October.	Presentation
Wong, RKH : Barrett's Esophagus - The pro's and con's of screening and surveillance. GI Grand Rounds and Case Presentations, University of Colorado, Denver CO, 2002 October.	Presentation
Wong, RKH : Barrett's Esophagus - What's important and what's not. GI Grand Rounds and Case Presentations, The Lahey Clinic, Boston MA, 2002 October.	Presentation
Wong, RKH : Barrett's Esophagus - What's important and what's not. Duke-UNC Medical Meeting, Myrtle Beach SC, 2003 May.	Presentation
Wong, RKH : Barrett's Esophagus - What's important and what's not. Henry Ford Hospital, Detroit MI, 2003 January.	Presentation
Wong, RKH : Barrett's Esophagus - What's important and what's not. GI Grand Rounds, Columbia University School of Medicine, New York NY, 2003 February.	Presentation
Wong, RKH : Barrett's Esophagus - What's important and what's not. GI Grand Rounds, University of Connecticut, Hartford CT, 2003 April.	Presentation
Wong, RKH : Consultant for Case Presentations. Gastroenterology Service, Yale Medical Center, New Haven CT, 2002 October.	Presentation
Wong, RKH : Extraesophageal manifestations of GERD. University of South Florida Symposium, Sarasota FL, 2002 November.	Presentation

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CITATION	TYPE
Wong, RKH : Medical therapy of GERD. GI Grand Rounds, Eisenhower Medical Center, Augusta GA, 2003 April.	Presentation
Wong, RKH : Non-cardiac chest pain. University of South Florida Symposium, Sarasota FL, 2002 November.	Presentation
Wong, RKH : NSAID-induced toxicity. University of South Florida Symposium, Sarasota FL, 2002 November.	Presentation
Wong, RKH : Role of H. Pylori in GERD. Pri-Med Symposium, Washington Convention Center, Washington DC, 2002 November.	Presentation
Wong, RKH : Screening and surveillance in Barrett's Esophagus. University of South Florida Symposium, Sarasota FL, 2002 November.	Presentation
Wong, RKH : The acute abdomen. 38th Parallel Medical Society Meeting, U.S. Army Forces, Seoul Korea, 2003 April.	Presentation
Wong, RKH : The Burning esophagus: Pathophysiology and new therapies for dousing the flames. Grand Rounds, University of Georgia School of Medicine, Augusta GA, 2003 April.	Presentation
Wong, RKH : The burning esophagus: Pathophysiology and treatment in dousing the flames. Grand Rounds, Rush Presbyterian Medical Center, Chicago IL, 2003 February.	Presentation
Wong, RKH : The burning esophagus: Pathophysiology and treatment of GERD. Grand Rounds, 9th Annual Robert E. Crozier Lecture in Medicine, The Lahey Clinic, Boston MA, 2002 October.	Presentation
Wong, RKH : The revolution that Barrett started. Medical College of Ohio, Toledo OH, 2003 January.	Presentation
Wong, RKH : Treatment of severe erosive esophagitis. Pri-Med Symposium, Washington Convention Center, Washington DC, 2002 November.	Presentation
<b><u>General Medicine Service</u></b>	
Bautista, L, PG O'Malley, JE Atwood, AJ Taylor : Association between mild chronic inflammation, blood pressure, and pulse pressure in normotensive subjects. American Heart Association Epidemiology Meeting, 2003 Spring.	Abstract
Berbano, E, PG O'Malley, K Abbott, DL Jones : Prevalence of microalbuminemia among patients with chronic renal insufficiency. National ACP Meeting, Army Chapter, 2002 November.	Abstract
Cloonan, C, HE Fauver, HC Holloway, DR Hospenthal, J Hutton, E Lewis, VE Madrigal, B Maliner, M Nelson, PC Reynolds, M Staunton, BA Wayne, MJ Roy : Military unique curriculum - Identifying and prioritizing content. Mil Med, 168:41-45, 2003.	Publication
Denton, GD, LN Pangaro, AC Wimmer, S Durning, PA Hemmer : Is a pre-clerkship examination equivalent to the pre-third year GPA and USMLE step one as a predictor of performance on the third year Internal Medicine clerkship? (poster). Society of General Internal Medicine Annual Meeting, Vancouver BC Canada, 2003 May.	Presentation
Durning, SJ, LN Pangaro, GD Denton, PA Hemmer, A Wimmer, T Grau, M Gaglione, L Moores : Inter-site consistency as a measurement of programmatic evaluation in a medicine clerkship with multiple geographically separated sites. Association for Medical Education in Europe Annual Meeting, Bern Switzerland, 2003 September.	Abstract
Durning, SJ, LN Pangaro, PA Hemmer, GD Denton, A Wimmer, T Grau, M Gaglione, L Moores : Inter-site consistency as a measurement of programmatic evaluation in a medicine clerkship with multiple geographically separated sites. Northeast GEA, Boston MA, 2003 March.	Abstract



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CITATION	TYPE
Durning, SJ, LN Pangaro, PA Hemmer, GD Denton, A Wimmer, T Grau, M Gaglione, L Moores : What contributes to the variance In NBME subject examination performance and recommended teacher grades - A 10-year analysis (poster). Association for Medical Education in Europe Annual Meeting, Bern Switzerland, 2003 September.	Presentation
Durning, SJ, PA Hemmer, LN Pangaro : How to evaluate your course or clerkship. Association for Medical Education in Europe Annual Meeting, Bern Switzerland, 2003 September.	Presentation
Elnicki, DM, PA Hemmer, MM Udden, R Wong, M Battistone, TA Albritton, CH Griffith : Does being a clerkship director benefit academic career advancement - Results of a national survey. Teach Learn Med, 15:21-24, 2003.	Publication
Gardner, J, RV Gibbons, T Hooper, et al : Identifying new diseases and their causes - The dilemma of illnesses in Gulf War veterans. Mil Med, 168(3):186-193, 2003 March.	Presentation
Gibbons, RV : Update of WRAIR tetravalent dengue vaccine development. WHO Task Force on Clinical Trials of Dengue Vaccines, Denver CO, 2002 November.	Presentation
Gibbons, RV : Update on dengue and dengue vaccine development. Army ACP, Crystal City VA, 2002 November.	Presentation
Gibbons, RV : Rabies. Therapy of Infectious Diseases, L Baddour & S Gorback eds, WB Saunders, New York NY, 2003.	Publication
Gibson, K : Crisis Management Seminar. Navy Postgraduate School (NPG), Monterey CA, 2003 February.	Presentation
Gibson, K : Crisis Management Seminar - Orientation Course for new general and SES officers. Washington DC, 2003 July.	Presentation
Gibson, K : Crisis Management Seminar - Spouses Seminar. Navy Postgraduate School (NPG), Monterey CA, 2003 February.	Presentation
Gibson, K : Crisis Management Seminar - USN Flag Orientation Course. Greensboro NC, 2003 August.	Presentation
Gibson, K : Executive Business Course. Command Naval AirLand (CNAL), Commander's Conference, Norfolk VA, 2003 September.	Presentation
Gibson, K : Executive Business Course. Monterey CA, 2003 May.	Presentation
Gibson, K : Executive Business Course - Executive Health Brief. Center for Executive Leadership, NPG, Monterey CA, 2003 May.	Presentation
Gibson, K : Wellness Brief. Navy Flag Orientation Course, Washington DC, 2003 July.	Presentation
Gibson, K : Wellness Brief - Spouses. Command Naval AirLand (CNAL), Commander's Conference, Norfolk VA, 2003 September.	Presentation
Hatzigeorgiou, C, JL Jackson : HMG CoA reductase inhibitors and osteoporosis- A meta-analysis. Army ACP National Meeting, Washington DC, 2002 November.	Abstract
Hatzigeorgiou, C, JL Jackson : HMG CoA reductase inhibitors and osteoporosis- A meta-analysis. Society of General Internal Medicine Annual Meeting, Vancouver BC Canada, 2003 May.	Abstract
Hauer, K, PA Hemmer, C Grum, RY Wong : A descriptive study of written H & P requirements in core Internal Medicine clerkships. Clerkship Directors in Internal Medicine Annual Meeting, Washington DC, 2002 October.	Abstract

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CITATION	TYPE
Hemmer, P : 5th Annual CDIM review of medical education - What are we doing?. Clerkship Directors in Internal Medicine Annual Meeting, Washington DC, 2002 October.	Presentation
Hemmer, P : Medical Education Review. Grand Rounds, State University of New York, Upstate Medical Campus, Syracuse NY, 2002 December.	Presentation
Hemmer, P : Preceptor handbook of core clerkship student skills (poster). Association for Medical Education in Europe Annual Meeting, Bern Switzerland, 2003 September.	Presentation
Hemmer, P, MJ Battistone : Implementing RIME and formal evaluation sessions on clinical clerkships - A primer for new clerkship directors. Clerkship Directors in Internal Medicine Annual Meeting, Washington DC, 2002 October.	Presentation
Hemmer, PA, C Griffith, DM Elnicki, M Fagan : The Internal Medicine clerkship in the clinical education of medical students. Am J Med, 115:423-427, 2003.	Publication
Hunt, ME, PG O'Malley, I Feuerstein, AJ Taylor : The metabolic "score" predicts subclinical atherosclerosis independent of fasting serum LDL - Evidence supporting inclusion of the metabolic syndrome as a component within the NCEP ATP III Guidelines. Coron Artery Dis, 14(4):317-322, 2003 June.	Publication
Jackson, JL : Satisfaction - A new model. Army ACP National Meeting, Washington DC, 2002 November.	Abstract
Jackson, JL : Structural equation modeling. National SGIM Meeting, Vancouver Canada, 2003 May.	Presentation
Jackson, JL, J Chamberlin, K Kroenke : Gender and symptoms in primary care. Psychosomatics, 44(5):359-366, 2003.	Publication
Jackson, JL, PG O'Malley, C Hatzigeorgiou, E Berbano : Workshop on how to perform and critically appraise a meta-analysis. National SGIM Meeting, Vancouver Canada, 2003 May.	Presentation
Jackson, JL, PG O'Malley, K Kroenke : Radiographic evaluation of acute knee pain. Ann Intern Med, 139:575-588, 2003.	Publication
Jackson, JL, PG O'Malley, K Kroenke : The management of acute knee pain in primary care. Ann Intern Med, 139:575-588, 2003.	Publication
Jackson, JL, PG O'Malley, L Sessums, M Diemer, E Berbano : Tricyclics and chronic headache. Cochrane Collaboration, Working Group, 2003.	Presentation
Jackson, JL, PG O'Malley, P Hemmer, L Inouye, L Pangaro, J Tofferi, CC Engel, D Omori, K David-Bajar, M Roy : Measuring outcomes for military medical education. Mil Med, 168(9):51-58, 2003.	Publication
Jackson, JL, PG O'Malley, S Salerno, K Kroenke : The teacher and learner interactive assessment system - A new tool to qualitatively assess learner-teacher interaction. Teach Learn Med, 14:249-256, 2002 Fall.	Presentation
Jackson, JL, PG O'Malley, SM Salerno, K Kroenke : The teacher and learner interactive assessment system (TeLIAS) - A new tool to assess teaching behaviors in the ambulatory setting. Teach Learn Med, 14(4):249-256, 2002 Fall.	Publication
Laughlin, LW, MJ Roy : Executive Summary. Mil Med, 168:102, 2003.	Publication
Lee, TC, PG O'Malley, I Feuerstein, AT Taylor : The prevalence and severity of coronary artery calcification on coronary computed tomography in black and white subjects. , 2003.	Presentation
Mark, DB, LJ Shaw, MS Lauer, PG O'Malley, P Heidenreich : Is atherosclerosis imaging cost-effective?. J Am Coll Cardiol, 41(11):1906-1917, 2003 June.	Presentation

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CITATION	TYPE
McQuiston, JH, RV Gibbons, R Velic, et al : Investigation of a focus of Q fever in a non-farming population in the Federation of Bosnia and Herzegovina. , 2003 June.	Presentation
McQuiston, JH, RV Gibbons, R Velic, WL Nicholson, L Castrodale, SH Wainright, TJ Vanniewenhoven, EW Morgan, L Arapovic, A Delilic, M O'Reilly, T Bajrovic : Investigation of a focus of Q fever in a non-farming population in the Federation of Bosnia and Herzegovina. Ann N Y Acad Sci, 990:229-232, 2003.	Publication
O'Malley, PG, AJ Taylor : Response to letters regarding the efficacy of EBCT to motivate behavioral change. JAMA, 2003 September.	Publication
O'Malley, PG, E Berbano : Efficacy of case-method learning in general practice for secondary prevention in patients with coronary artery disease - randomized controlled study. Commentary in "Evidence Based Medicine", 2003.	Publication
O'Malley, PG, E Berbano : Efficacy of case-method learning in general practice for secondary prevention in patients with coronary artery disease - randomized controlled study. Kiessling and Henrickson BMJ, 325:877, 2002 (FY03).	Publication
O'Malley, PG, IM Feuerstein, AJ Taylor : The impact of Electron Beam Tomography, with or without case management, on motivation to change, behaviors, and the cardiovascular risk profile - A randomized controlled trial. JAMA, 2003.	Presentation
Palma, J, MJ Roy : Certification in military medicine working group - Certification in military medicine. Mil Med, 168:59-65, 2003.	Publication
Papp, KK, MJ Battistone, S Durning, DM Elnicki, PA Hemmer : CDIM abstracts -1995-2000. Clerkship Directors in Internal Medicine Annual Meeting, Washington DC, 2002 October.	Abstract
Papp, KK, MJ Battistone, S Durning, DM Elnicki, PA Hemmer : Title not available. Clerkship Directors in Internal Medicine Annual Meeting, Washington DC, CDIM Abstracts, 1995-2000, 2002 October.	Abstract
Pinholt, E : Teaching geriatrics - Seven-Part Seminar Series. WRAMC, Washington DC, 2003 March-May.	Presentation
Posley, K : The future of clinical General Internal Medicine - a hospitalist's perspective. SGIM Mid-Atlantic Regional Meeting Panel, Baltimore MD, 2003 May.	Presentation
Rinaldo, J : Improving military-NGO interactions in post conflict humanitarian actions. 17th Annual Conference of Military Medicine, USUHS, Bethesda MD, 2003 June.	Presentation
Rinaldo, J : Training in humanitarian assistance and refugee health for military Internal Medicine residents. American College of Physicians and American Society of Internal Medicine, 2002 November.	Presentation
Rinaldo, J : Training in humanitarian medicine for Internal Medicine residents and fellows in a U.S. Army Medical Center Training Program. Johns Hopkins University, 2003 May.	Presentation
Rinaldo, J : War and conflict - retooling military medical forces to take on unique public health roles. Psychological Factors in Health and Illness, Johns Hopkins University School of Public Health Summer Symposium, 2003 June.	Presentation
Roy, M : Diagnosing and treating depression in the primary care setting. Bridging the Gap, Speaker's Training, Baltimore MD, 2003 September.	Presentation
Roy, M : Diagnosing and treating depression in the primary care setting - Healthcare disparity, depression, and chronic diseases. Bridging the Gap, National Medical Association Conference, Philadelphia PA, 2003 August.	Presentation
Roy, M : Diagnosing depression and primary care. Bridging the Gap National Advisory Board Meeting, Baltimore MD, 2003 January.	Presentation

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CITATION	TYPE
Roy, M : Diagnosing depression in primary care. Baltimore MD, 2003 May.	Presentation
Roy, M : Diagnosing depression in primary care. National Hispanic Medical Association Bridging the Gap, Train the Trainer Workshop, American Psychiatric Association Annual Meeting, San Francisco CA, 2003 May.	Presentation
Roy, M : Evolving to meet new challenges. National Defense Medical School, Tokorozawa Japan, 2003 June.	Presentation
Roy, M : Increasing the diagnosis of depression and anxiety in the primary care setting. McLean VA, 2003 April.	Presentation
Roy, M : Increasing the diagnosis of depression and anxiety in the primary care setting. Lanham-Seabrook MD, 2003 May.	Presentation
Roy, M : Increasing the diagnosis of depression and anxiety in the primary care setting. Bethesda MD, 2003 April.	Presentation
Roy, M : Lessons learned from mail-disseminated cases of anthrax. 2nd Congress of the Physicians of Macedonian Preventive Medicine, Ohrid Macedonia, 2002 October.	Presentation
Roy, M : Life during wartime - Diagnosis and management of depression, anxiety, and PTSD. Dewitt Army Community Hospital Grand Rounds, Fort Belvoir VA, 2003 April.	Presentation
Roy, M : Management of potential exposure to biological agents - Most likely bioterror pathogens. National Defense Medical School, Tokorozawa Japan, 2003 June.	Presentation
Roy, M : Medical aspects of chemical warfare. National Defense Medical School, Tokorozawa Japan, 2003 June.	Presentation
Roy, M : Medical effects of ionizing radiation. National Defense Medical School, Tokorozawa Japan, 2003 June.	Presentation
Roy, M : Military Medicine - Mission, structure, and evolution. National Defense Medical School, Tokorozawa Japan, 2003 June.	Presentation
Roy, M : Psychological sequelae of terrorism and war. 2nd Congress of the Physicians of Macedonian Preventive Medicine, Ohrid Macedonia, 2002 October.	Presentation
Roy, M : Responding to a crisis. National Defense Medical School, Tokorozawa Japan, 2003 June.	Presentation
Roy, M : Responding to terrorist attacks - Hands-on experience for internists. 19th Annual Army American College of Physicians Meeting, Arlington VA, 2002 November.	Presentation
Roy, M : Screening and diagnosing depression in the primary care setting. Bridging the Gap Workshop, American Academy of Family Physicians Annual Scientific Assembly, San Diego CA, 2002 October.	Presentation
Roy, M : Teaching military medicine in the clinic, in the hospital, and in the field. National Defense Medical School, Tokorozawa Japan, 2003 June.	Presentation
Roy, M : Tools to diagnose and manage depression. Albert Einstein Health Network Grand Rounds, Philadelphia PA, 2003 January.	Presentation
Roy, M : War in the Persian Gulf and soldier's health - Lessons learned. Kimbrough Ambulatory Care Center, Fort Meade MD, 2003 June.	Presentation
Roy, M : War in the Persian Gulf and soldier's health - Lessons learned. National Defense Medical School, Tokorozawa Japan, 2003 June.	Presentation

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CITATION	TYPE
Roy, M : War in the Persian Gulf and soldier's health - Lessons learned. Ground Self Defense Force Medical School, Tokyo Japan, 2003 June.	Presentation
Roy, M, PA Hemmer, D Omori, G Adamo, N Aronson, R Hawkins : Bioterrorist attacks - Hands-on experience for internists. American College of Physicians, Army Chapter, Annual Meeting, Crystal City VA, 2002 November.	Presentation
Roy, MJ : Bioterrorism. Combat Medicine (G. Tsokos, ed.), Humana Press, Totawa NJ, 2003.	Publication
Roy, MJ : Enhancing readiness - Implementing change in military medical education. Mil Med, 168(suppl):1-65, 2003.	Publication
Roy, MJ, AJ Seidman, C Lucas, K Kroenke, JE Herbers : Improving patient satisfaction with the transfer of care - A randomized controlled trial. J Gen Intern Med, 18:364-369, 2003.	Publication
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Abbott, KC, JR Bucci, LY Agodoa : Total hip arthroplasty in chronic dialysis patients in the United States. <i>J Nephrol</i> , 16(1):34-39, 2003 January-February.	Publication
Abbott, KC, LY Agodoa, PG O'Malley : Hospitalized Psychoses after Renal Transplantation in the U.S.. <i>J Am Soc Nephrol</i> , 14(6):1628-1635, 2003 June.	Publication
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Abbott, KC, P Hsieh, D Cruess, LY Agodoa, PG Welch, AJ Taylor, CM Yuan : Hospitalized valvular heart disease in patients on renal transplant waiting list - Incidence, clinical correlates and outcomes. <i>Clin Nephrol</i> , 59(2):79-87, 2003 February.	Publication
Abbott, KC, R Viola, LY Agodoa : Hospitalizations for Poisonings after Renal Transplantation in the U.S.. <i>Biomed Central Nephrol</i> , 3(1):10, 2002 November.	Publication
Abbott, KC, RJ Oglesby, LY Agodoa : Hospitalized avascular necrosis after renal transplantation in the United States. <i>Kidney Int</i> , 62(6):2250-2256, 2002 December.	Publication
Bucci, JR, CS Matsumoto, SJ Swanson, LY Agodoa, KC Holtzmuller, TG Peters, KC Abbott : Donor hepatitis C seropositivity - Clinical correlates and effect on early graft and patient survival in adult cadaveric kidney transplantation. <i>J Am Soc Nephrol</i> , 13(12):2974-2982, 2002 December.	Publication
Bucci, JR, RJ Oglesby, LY Agodoa, KC Abbott : Total Hip Arthroplasty after Renal Transplantation in the United States (poster). <i>ASN, Philadelphia PA</i> , 2002 November.	Presentation
Bucci, JR, RJ Oglesby, LY Agodoa, KC Abbott : Hospitalizations for total hip arthroplasty after renal transplantation in the U.S.. <i>Am J Transplant</i> , 2(10):999-1004, 2002 November.	Publication

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Glanton, CW, LY Agodoa, KC Abbott : Impact of Renal Transplantation on Survival in ESRD Patients with elevated Body Mass Index. <i>Kidney Int</i> , 63:647-653, 2003.	Publication
Glanton, CW, PB Hshieh, D Cruess, LY Agodoa, CM Yuan, KC Abbott : Factors Associated with Survival in Obese End Stage Renal Disease Patients in the United States. <i>Ann Epidemiol</i> , 13:136-143, 2003.	Publication
Lee, JY, KC Abbott : Hand atrophy associated with arteriovenous fistula placement (poster). NKF, Dallas TX, 2003 April.	Presentation
Oliver, JD III, JL Atkins, JL Schooley, ER Morris, L Ma, TB Bentley, MB Pamnani : Interstitial concentrations during hemorrhagic shock. <i>Shock</i> , 19 Suppl:53, 2003.	Abstract
Reynolds, JC, LY Agodoa, CM Yuan, KC Abbott : Hospitalized HUS/TTP after Renal Transplantation in the United States (poster). American Transplant Congress, Washington DC, 2003 June.	Presentation
Shorr, AF, KC Abbott, LY Agodoa : Acute respiratory distress syndrome after kidney transplantation - Epidemiology, risk factors, and outcomes. <i>Crit Care Med</i> , 31(5):1325-1330, 2003 May.	Publication
Simon, J : Concurrent beer potomania and SIADH in a 47-year-old white male (poster). NKF, Dallas TX, 2003 April.	Presentation
Stiles, K, M Moffat, LY Agodoa, KC Abbott : Renal Cell Carcinoma as a cause of End Stage Renal Disease in the United States (poster). ASN, Philadelphia PA, 2002 November.	Presentation
Stiles, KP, MJ Moffatt, LY Agodoa, SJ Swanson, KC Abbott : Renal cell carcinoma as a cause of end-stage renal disease in the United States - Patient characteristics and survival. <i>Kidney Int</i> , 64(1):247-253, 2003 July.	Publication
Swanson, SJ, AD Kirk, CW Ko, CA Jones, LY Agodoa, KC Abbott : Impact of HIV seropositivity on graft and patient survival after cadaveric renal transplantation in the United States in the pre highly active antiretroviral therapy (HAART) era: an historical cohort analysis of the United States Renal Data System. <i>Transpl Infect Dis</i> , 4(3):144-147, 2002 October-November.	Publication
Trespalacios, FC, AJ Taylor, LY Agodoa, GL Bakris, KC Abbott : Heart failure as a cause for hospitalization in chronic dialysis patients. <i>Am J Kidney Dis</i> , 41(6):1267-1277, 2003 June.	Publication
Trespalacios, FC, AJ Taylor, LY Agodoa, KC Abbott : Heart Failure as an Etiology for Hospitalization in Chronic Dialysis Patients in the United States (poster). ASN, Philadelphia PA, 2002 November.	Presentation
Trespalacios, FC, AJ Taylor, LY Agodoa, KC Abbott : Incident acute coronary syndromes in chronic dialysis patients in the United States (poster). ASN, Philadelphia PA, 2002 November.	Presentation
Trespalacios, FC, AJ Taylor, LY Agodoa, KC Abbott : Incident acute coronary syndromes in chronic dialysis patients in the United States. <i>Kidney Int</i> , 62(5):1799-1805, 2002 November.	Publication
Viola, R, K Abbott, P Welch, R McMillan, A Sheikh, C Yuan : A multi-disciplinary program for achieving lipid goals in chronic hemodialysis patients. <i>BMC Nephrol</i> , 3(1):9, 2002 November.	Publication
Yuan, CM, Y Wang, JF Schooley, V Bernet, KC Abbott, MB Pamnani : Na <sup>+</sup> ,K <sup>+</sup> ATPase Inhibitor in Type 2 Diabetes Mellitus Patients with and without Clinical Nephropathy (poster). Clinical Research 2003 Meeting, Baltimore MD, 2003 March.	Presentation

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CITATION	TYPE
<b><u>Pulmonary &amp; Critical Care Medicine Service</u></b>	
Arora, R, C Lettieri : Effects of residency of physical fitness among military physicians. American College of Physicians, Army Chapter, Annual Meeting, Crystal City VA, 2002 November.	Presentation
Carlson, D, C Lettieri : Utility of the ACC/AHA recommendations on preoperative evaluations (poster). American College of Physicians, Army Chapter, Annual Meeting, Crystal City VA, 2002 November.	Presentation
Carson, SB, AF Shorr : The effect of definitions on outcomes from critical care research. Curr Opinion Crit Care, 9:308-315, 2003.	Publication
Helman, DL, A Sullivan, ST Kariya, SH Deering, N Hueppchen, AF Shorr : Management of idiopathic pulmonary hemosiderosis in pregnancy - Report of 2 cases. Respirology, 8:398-400, 2003.	Publication
Helman, DL, JH Sherner, TM Fitzpatrick, ME Calendar, AF Shorr : Effect of standardized orders and provider education on head-of-bed positioning in mechanically ventilated patients. Crit Care Med, 31:2291-2301, 2003.	Publication
Helman, DL, RM Peckham, AF Shorr : Clinical criteria for a diagnosis of idiopathic pulmonary fibrosis - A study of interobserver variability. American College of Chest Physicians National Meeting, San Diego CA, 2002 November.	Presentation
Holley, AB, JF Collen, AF Shorr, LK Moores : Troponin T levels are associated with ventricular strain in pulmonary embolism. Am J Resp Crit Care Med, 167(Suppl):A282, 2003.	Abstract
Hospenthal, DL, CJ Lettieri, JE Moon, PW Hickey, MR Gray, BW Berg : Prevalence of Leptospiral antibody in U.S. Army blood donors in Hawaii. Am J Trop Med Hyg, 67(Suppl):192, 2002 (FY03).	Abstract
Hospenthal, DR, CJ Lettieri, JE Moon, PW Hickey, MR Gray, BW Berg : Prevalence of leptospiral antibody in U.S. Army blood donors in Hawaii. 51st Annual Meeting of American Society Tropical Medicine Hygiene, Denver CO, 2002 November.	Presentation
Humphreys, CW, LK Moores, AF Shorr : Cost minimization analysis of two algorithms for diagnosing acute pulmonary embolism. Am J Resp Crit Care Med, 167(Suppl):A281, 2003.	Abstract
Humphreys, CW, LK Moores, AF Shorr : Cost-minimization analysis of two algorithms for diagnosing PE. American Thoracic Society International Scientific Conference, Seattle WA, 2003 May.	Presentation
Humphreys, CW, LK Moores, AF Shorr : Cost-minimization analysis of two algorithms for diagnosing PE. Army ACP Annual Meeting, Arlington VA, 2002 November.	Presentation
Jackson, EL, R Bridwell, LK Moores : A novel diagnostic modality for acute pulmonary embolism - 99mTc-AcuTect scintigraphy in a patient with acute PE. Chest, 122(4 Suppl):237S, 2002 December.	Abstract
Jackson, KE, WL Jackson Jr. : The right to health and the nevirapine case in South Africa [letter]. N Engl J Med, 348:2470-2471, 2003.	Publication
Jackson, W, L Moores : Recruitment maneuvers should be done routinely in patients with acute lung injury/ARDS - Lung recruitment and the ARDSNet ALVEOLI Trial (Pro). CHEST Clinical Controversy Pro-Con Session, American College of Chest Physicians, San Diego CA, 2002 November.	Presentation
Jackson, WL, AF Shorr : The yield of lumbar puncture for nosocomial meningitis in the medical intensive care unit. Crit Care Med, 30:A78, 2002 (FY03).	Abstract
Jackson, WL, Jr. : Management of acute renal failure. Ann Intern Med, 139:529-530, 2003.	Publication
Kristo, D, T Andrada, A Eliasson : Telemedicine in the sleep laboratory - A carefully worked out business plan is essential to justify the investment. Advance for Managers in Respiratory Care, 12(6):50, 2003.	Publication

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Lettieri, C, B Berg : Clinical features of non-Hodgkin's lymphoma presenting with acute liver failure - A report of 5 cases and review of published experience. Am J Gastroenterol, 98(7):1641-1646, 2003 July.	Publication
Lettieri, C, G Veerappan, A Shorr : Outcomes of surgical lung biopsy in patients requiring mechanical ventilation. Critical Care Society, DC Chapter, 2003.	Presentation
Meoli, A, C Rosen, D Kristo, et al : Non-prescription treatments of snoring and obstructive sleep apnea - An evaluation of products with limited scientific evidence. Sleep, 26(5):619-624, 2003.	Publication
Meyerle, JH, AF Shorr : The use of Infliximab in cutaneous sarcoidosis. J Drugs Dermatol, 2:413-415, 2003.	Publication
Moores, LK : AcuTect in the diagnosis of acute clot. CHEST Plenary Presentation, San Diego CA, 2002 November.	Presentation
Moores, LK : Mentorship - Key features of an effective mentor and why you should have one. CHEST Post Graduate Course, San Diego CA, 2002 November.	Presentation
Moores, LK : Venous Thromboembolism - Greatest hits (An update on new diagnostic tests in VTE). CHEST Panel Discussion, San Diego CA, 2002 November.	Presentation
Niven, AS, TJ Backenson, MD Goldman, OW Hnatiuk, IM Weisman : Resistance measured by forced oscillation (IOS) is mouthpiece dependent and reduced in normal subjects using a Free Flow mouthpiece. Am J Resp Crit Care Med, 167(7):A419, 2003.	Abstract
Parker, JM, BW Berg : Prevalence of hyperventilation in patients with vocal cord dysfunction. Chest, 122(4):185S, 2002 October.	Abstract
Perello, MM, J Gurevich, T Fitzpatrick, BW Berg, JM Parker : Clinical characteristics of vocal cord dysfunction in two military tertiary care facilities. Am J Resp Crit Care Med, A788, 2003 April.	Abstract
Pierce, FN, D Kristo, JS Wink, AH Eliasson, A Khramtsov, ML Guerrero, Y Taylor, TF Andrada : Comparison in CPAP adherence among UARS patients split versus full night positive airway titration. American Academy of Sleep Medicine, Chicago IL, 2003 May.	Abstract
Salerno, SM, PG O'Malley, LN Pangaro, GA Wheeler, LK Moores, JL Jackson : Faculty development seminars based on the one-minute preceptor improve feedback in the ambulatory setting. J Gen Intern Med, 17(10):779-787, 2002 October.	Publication
Shorr, AF : Methicillin-resistant staphylococcus aureus in the intensive care unit - Attributable mortality and the cost of inappropriate treatment choices. Informed Decisions, 1:7-12, 2003.	Publication
Shorr, AF, CW Humphreys, DL Helman : New choices for central venous catheters - Potential financial implications. Chest, 124(1):275-284, 2003 July.	Publication
Shorr, AF, DB Davies, DL Helman, SA Nathan : Short-term outcomes for patients with sarcoidosis following lung transplantation. American Thoracic Society International Scientific Conference, Seattle WA, 2003 May.	Abstract
Shorr, AF, DB Davies, DL Helman, SD Nathan : Predicting mortality in patients with sarcoidosis awaiting lung transplantation. American College of Chest Physicians National Meeting, San Diego CA, 2002 November.	Abstract
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Shorr, AF, KC Abbott : Impact of acute respiratory distress syndrome on mortality following kidney transplantation. American Thoracic Society International Scientific Conference, Seattle WA, 2003 May.	Abstract
Shorr, AF, KC Abbott, LY Agadoa : Outcomes for patients with ARDS after renal transplantation. American College of Chest Physicians National Meeting, San Diego CA, 2002 November.	Abstract
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Shorr, AF, LC Abbott, LY Agadoa : Acute respiratory distress syndrome following lung transplantation. American College of Chest Physicians National Meeting, San Diego CA, 2002 November.	Presentation
Shorr, AF, SA Nasraway, N O'Grady, VH Le, SK Cammarata : Linezolid does not increase risk for thrombocytopenia in nosocomial pneumonia patients. American Thoracic Society International Scientific Conference, Seattle WA, 2003 May.	Abstract
Taylor, Y, D Kristo, A Eliasson : A comparison of telemedicine to traditional care among individuals with obstructive sleep apnea syndrome. American Academy of Sleep Medicine, Chicago IL, 2003 May.	Abstract
Taylor, YL, A Eliasson, D Kristo, A Andrada, T Bigott, P Ephraim : A comparison between a telemedicine and traditional management model of care with nasal continuous positive airway pressure use among individuals with obstructive sleep apnea syndrome (Poster). American Telemedicine Association 2003 Annual Meeting, 2003 April.	Presentation
Taylor, YL, A Eliasson, D Kristo, A Andrada, T Bigott, P Ephraim, R Howard : Can telemedicine improve compliance use with nasal CPAP? (Poster). American Professional Sleep Societies, 2003 June.	Presentation
Verappan, G, C Lettieri : Non-small cell lung cancer presenting as a malar mass. American College of Physicians, Army Chapter, Annual Meeting, Crystal City VA, 2002 November.	Presentation
Wink, JS, LK Moores, KM Woods : Alternative diagnosis in suspected pulmonary embolism - Value of CT-angiography. Chest, 122(4 Suppl):58S, 2002 (FY03).	Abstract
Wood, KM, JF Colleen, AF Shorr, LK Moores : Validation of clinical prediction scores in pulmonary embolism. American College of Chest Physicians National Meeting, San Diego CA, 2002 November.	Presentation
Woods, KM, JF Collen, AF Shorr, LK Moores : Validation of clinical prediction scores in pulmonary embolism. Chest, 122(4 Suppl):59S, 2002 October.	Abstract
Zisman, DA, AF Shorr, JP Lynch : Sarcoidosis involving the musculoskeletal system. Semin Respir Crit Care Med, 23:555-570, 2002 (FY03).	Publication
<b><u>Rheumatology Service</u></b>	
Corey, WW, RJ Oglesby : Thrombotic thrombocytopenic purpura in systemic lupus erythematosus. Army ACP, Crystal City VA, 2002 November.	Presentation
Delaney, NR, JD Roebuck : A diagnostic challenge - Systemic lupus erythematosus vs. amyopathic dermatomyositis. Army ACP, Crystal City VA, 2002 November.	Presentation
Gilliland, WR, NR Delaney, AB Holley : A 41 year-old active duty U.S. Air Force enlisted man with a 3-week history of fevers, arthralgias, and myalgias. Mil Med, 168(1):82-85, 2003.	Publication



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Harner, KC, WR Gilliland : Arthritis secondary to systemic lupus erythematosus (SLE)...or not - A patient with known SLE now with positive gonorrheal culture. Army ACP, Crystal City VA, 2002 November.	Presentation
Juang, YT, K Tenbrock, MP Nambiar, MF Gourley, GC Tsokos : Defective production of functional 98-kDa form of Elf-1 is responsible for the decreased expression of TCR zeta-chain in patients with systemic lupus erythematosus. J Immunol, 169(10):6048-6055, 2002 November.	Publication
McKinley, BT, JD Roebuck : Rheumatology quiz: catheter associated vascular insufficiency. Res Staff Physician, 49(2):37, 48, 2003.	Publication
McKinley, BT, RJ Oglesby : Cryoglobulinemia vasculitis in a patient with long standing rheumatoid arthritis and hepatitis B surface antigenemia. Army ACP, Crystal City VA, 2002 November.	Presentation
Nambiar, MP, CU Fisher, A Kumar, CG Tsokos, VG Warke, GC Tsokos : Forced expression of the Fc receptor gamma-chain renders human T cells hyperresponsive to TCR/CD3 stimulation. J Immunol, 170(6):2871-2876, 2003 March.	Publication
Nambiar, MP, JP Mitchell, RP Ceruti, MA Malloy, GC Tsokos : Prevalence of T cell receptor zeta chain deficiency in systemic lupus erythematosus. Lupus, 12(1):46-51, 2003.	Publication
Peckham, R, J Mitchell : Metastatic melanoma of unknown primary masquerading as Reiter's Syndrome. Army ACP, Crystal City VA, 2002 November.	Presentation
Roebuck, JD, RJ Oglesby : A 36 year-old military recruit with recurrent myalgias and weakness. Mil Med, 168(4):348-350, 2003 April.	Publication
Steinberg, BR, JD Roebuck : Therapeutic dilemma - Pneumonia in an immunosuppressed patient with hepatitis C associated vasculitis. Army ACP, Crystal City VA, 2002 November.	Presentation
Tsokos, GC, MP Nambiar, K Tenbrock, YT Juang : Re-wiring the T-cell - Signaling defects and novel prospects for the treatment of SLE. Trends Immunol, 24(5):259-263, 2003 May.	Publication
Tsokos, GC, MP Nambiar, YT Juang : Activation of the Ets transcription factor Elf-1 requires decreased TCR zeta chain gene expression in patients with systemic lupus erythematosus. Ann N Y Acad Sci, 987:240-245, 2003 April.	Publication

### **DEPARTMENT OF NEUROLOGY**

Arden, DL, LM Ryan, MB Sparling, KS Comins, DB Rayburn, Z Sun, RJ Labutta : Telemedicine Assessment of Neurobehavioral Consequences of Traumatic Brain Injury (poster). 8th Annual Meeting and Exposition, Orlando FL, 2003 April.	Presentation
Barner, KC, ME Landau, WW Campbell : A review of perioperative nerve injury to the lower extremities. J Clin Neuromusc Dis, 4:95-99, 2002 (FY03).	Publication
Barner, KC, ME Landau, WW Campbell : A review of perioperative nerve injury to the upper extremities. J Clin Neuromusc Dis, 4:117-123, 2003.	Publication
Campbell, WW, ME Landau : The Difference between Fibrillations and Positive Sharp Waves is due to Tissue Filtering. J Clin Neurophys, 20:201-206, 2003.	Abstract
Campbell, WW, ME Landau : The Difference between Fibrillations and Positive Sharp Waves is due to Tissue Filtering. Neurology, 20(3):201-206, 2003 May-June.	Abstract
Comins, KS, LM Ryan, MB Sparling, DL Warden : Neuropsychological, psychiatric, and demographic factors relate to postconcussion symptom reporting after traumatic brain injury. J Neuropsychiatry Clin Neurosci, 15(2):277, 2003.	Abstract

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Diaz, MI, ME Landau, KC Barner, WW Campbell : Effect of experimental error on ulnar across elbow nerve conduction velocity determinations. <i>Muscle Nerve</i> , 26:563, 2002 October-November.	Abstract
French, LM, LM Ryan, DL Warden : Characteristics of a group of military traumatic brain injury patients with somatoform symptoms. <i>J Neuropsychiatry and Clinical Neurosciences</i> , 15(2):277, 2003.	Abstract
French, LM, LM Ryan, DL Warden : Characteristics of a group of military traumatic brain injury patients with somatoform symptoms. <i>J Neuropsychiatry Clin Neurosci</i> , 15(2):277, 2003.	Publication
Jabbari, B : Power tools for your post-polio toolkit. The Polio Society's National Conference, 2002 October.	Presentation
Kudelko, K, ME Landau, WW Campbell : Muscle Hypertrophy in Kobberling-Dunnigan Syndrome: A Case report. <i>Muscle Nerve</i> , 2003.	Abstract
Labutta, RJ, RM Engler, JA Brooks, CD Petit, G Feolo : Smallpox vaccination – Incidence of Headache. <i>Headache</i> , 43(5):517, 2003.	Abstract
Landau, ME, KC Barner, WW Campbell : Optimal Distances for screening Ulnar Neuropathy at the Elbow. <i>Muscle Nerve</i> , 26:564, 2002 October-November.	Abstract
Landau, ME, KC Barner, WW Campbell : Optimal Screening Distance for Ulnar neuropathy at the elbow. <i>Muscle Nerve</i> , 27:570-574, 2003.	Publication
Landau, ME, MI Diaz, KC Barner, WW Campbell : Changes in nerve conduction velocity across the elbow due to experimental error. <i>Muscle Nerve</i> , 26(6):838-840, 2002 December.	Abstract
Landau, ME, MI Diaz, KC Barner, WW Campbell : Optimal Distance for Nerve Conductions: The 10 cm Rule in the 21st Century. <i>Muscle Nerve</i> , 26:593, 2002 October-November.	Abstract
Landau, ME, MI Diaz, KC Barner, WW Campbell : Changes in nerve conduction velocity across the elbow due to experimental error. <i>Muscle Nerve</i> , 26(6):838-840, 2002 December.	Publication
Landau, ME, MI Diaz, KC Barner, WW Campbell : Changes in Nerve conduction velocity across the elbow due to experimental error. <i>Muscle Nerve</i> , 26:838-840, 2002 December.	Publication
Landau, ME, MI Diaz, KC Barner, WW Campbell : Optimal distance for segmental nerve conduction studies revisited. <i>Muscle Nerve</i> , 27(3):367-369, 2003 March.	Publication
Landau, ME, MI Diaz, KC Barner, WW Campbell : Optimal Distance for Segmental Nerve Conduction Studies Revisited. <i>Muscle Nerve</i> , 27:367-369, 2003.	Publication
Marini, AM, JY Choi, RJ Labutta : Transient neurological deficits associated with carbamazepine-induced hypertension. <i>Clin Neuropharmacol</i> , 26:174-176, 2003.	Publication
Martin, EM, M Coyle, DL Warden, AM Salazar : A home program of rehabilitation for moderately severe traumatic brain injury patients (poster). 99th Annual Conference of the Maryland Nurse Association, 2002 October.	Presentation
Murray, ED, ME Landau, KC Barner, WW Campbell : The Cold Elbow Syndrome: Spurious Slowing of Ulnar Nerve Conduction Velocity. <i>Neurology</i> , 60 (suppl 1):A408-409, 2003.	Abstract
Potts, RE, KC Barner, ME Landau, WW Campbell : Body Mass Index as a Risk Factor for Ulnar neuropathy and Carpal tunnel syndrome. <i>Muscle Nerve</i> , 26:567, 2002 October-November.	Abstract
Riechers, R, ME Landau, G Farber, WW Campbell : Damage to Ulnar Sensory fibers in Martin-Gruber anastomosis due to bicipital tendon repair. <i>Muscle Nerve</i> , 2003.	Abstract

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Sartori, R, ME Landau, KC Barner, WW Campbell : A normal serum cobalamin level does not exclude neurological illness related to Vitamin B12 dysmetabolism. Neurology, 60 (suppl 1):A181, 2003.	Abstract
Sparling, MB, KS Komins, LM Ryan, RJ Labutta, DL Warden : Remote evaluations of postconcussion symptoms utilizing telemedicine technology. J Neuropsychiatry and Clinical Neurosciences, 15(2):279, 2003.	Abstract
Swanberg, MM, JL Cummings : Diagnosis and Treatment of Alzheimer's Disease. TEN, 5(3):55-62, 2003.	Abstract
Warden, DL : Evidence Based Guidelines for Neurobehavioral Consequences of TBI. USUHS Annual TBI Conference, Bethesda MD, 2003 June.	Presentation
Warden, DL : Evidence Based Guidelines for Neurobehavioral Consequences of TBI. Annual Williamsburg TBI Conference, Williamsburg VA, 2003 June.	Presentation
Warden, DL, LM Ryan, MB Sparling, KS Comins, DB Rayburn, Z Sun, RJ Labutta : Telemedicine assessment of neurobehavioral consequences of traumatic brain injury (poster). ATA 2003 8th Annual Meeting & Exposition, Orlando FL, 2003 April.	Presentation

### **DEPARTMENT OF NURSING**

: Development of an Army Nursing Practice Ethical Issues Scale. 16th Annual Pacific Nursing Research Conference, Honolulu HI, 2003 March.	Abstract
: Development of an Army Nursing Practice Ethical Issues Scale. 16th Annual Pacific Nursing Research Conference, Honolulu HI, 2003 March.	Presentation
: Musculoskeletal injury in AMEDD soldiers (poster). 6th Annual Force Health Protection Conference, U.S. Army Center for Health Promotion & Preventive Medicine, Albuquerque NM, 2003 August.	Presentation
Barajas, K, W Stewart, E Combs : The Army chemical/biological SMART (SMART-CB) team - The nurse's role. Critical Care Nursing Clinics of North America, 15(2):257-264, 2003.	Publication
Brosch, L : Military nursing outcomes database (MilNOD). Advancement for Nursing Science, Bethesda MD, 2003 September.	Presentation
Brosch, L, L Loan : Unit of analysis considerations in assessing staffing effectiveness and patient outcome indicator data. Eastern Nursing Research Society Annual Meeting, New Haven CT, 2003 March.	Abstract
Brown, CG : Testicular cancer - An overview. Medsurg Nurs, 12(1):37-43, 2003 February.	Publication
Coburn, P : Exercise and weight management behaviors of active duty health care personnel. Nursing Research Day 2002, WRAMC, Washington DC, 2002 December.	Presentation
Combs, E : Musculoskeletal injuries in AMEDD soldiers. 16th Annual Pacific Nursing Research Conference, Honolulu HI, 2003 March.	Abstract
Combs, E : Musculoskeletal injury in AMEDD soldiers. 16th Annual Pacific Nursing Research Conference, Honolulu HI, 2003 March.	Presentation
Combs, E : Walter Reed Army Medical Center Smallpox Vaccination Program, Lessons Learned (poster). AUSA Medical Symposium, San Antonio TX, 2003 June.	Presentation

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Jolivet, R : Contraceptive methods. Pregnant Soldiers' Workshop, WRAMC, Washington DC, 2003 September.	Presentation
Jolivet, R : Early-onset neonatal group B streptococcal infection - 2002 Guidelines for prevention. J Midwifery Women's Health, 47(6):435-446, 2002 November-December.	Publication
Keller, R : Psychological factors affecting those who handle human remains after mass disasters and their potential importance in the setting of modern terrorist attacks (Psychological Aspects of Terrorism). Nova Science, 2003.	Publication
Kenny, D : Research utilization of RNs in US Army hospitals. CAMC Institute 7th National Nursing Research Conference, Nursing Research for Practice - Past Present Future, White Sulphur Springs WV, 2002 November.	Abstract
Kenny, D : Research utilization of RNs in U.S. Army hospitals. Washington DC Chapter AORN, 2003 April.	Presentation
Kenny, D : Research utilization of RNs in U.S. Army hospitals. Center for Knowledge Transfer, Edmonton, Alberta Canada, 2002 November.	Presentation
Kenny, D : Research utilization of RNs in U.S. Army hospitals. 2002 Nursing Research Conference, Nursing Research for Practice - Past, Present and Future, White Sulphur Springs WV, 2002 November.	Presentation
Kenny, D : Research utilization of RNs in U.S. Army hospitals (poster). 108th Association of Military Surgeons of the U.S. (AMSUS) Conference, Louisville KY, 2002 November.	Presentation
Kenny, D : Research utilization of RNs in US Army hospitals. AMSUS 108th Annual Meeting, Karen Rieder Poster Session, Louisville KY, 2002 November.	Presentation
Kenny, D : Research utilization of RNs in US Army hospitals. CAMC Institute 7th National Nursing Research Conference, Nursing Research for Practice - Past Present Future, White Sulphur Springs WV, 2002 November.	Presentation
Lamp, C : Myocardial revascularization - Creating new pathways for coronary blood flow. Nursing 2003 Conference, Orlando FL, 2003 March.	Presentation
Miltner, RS : More than support - Nursing interventions provided to women in labor. J Obstet Gynecol Neonatal Nurs, 31(6):753-761, 2002 November-December.	Publication
Nolan-Polite, E : Antiretroviral adherence in a DOD environment. HIV Research - Past, Present and Future, WRAMC, Washington DC, 2002 November.	Presentation
Patrician, P : Medication error reporting - Anonymous versus formal reporting. 16th Annual Pacific Research Conference, Honolulu HI, 2003 March.	Abstract
Patrician, P : Medication error reporting and the work environment. Eastern Nursing Research Society Annual Meeting, New Haven CT, 2003 March.	Abstract
Patrician, P : Medication errors and nurse staffing - What's the connection? (poster). Annual Academy Health Meeting, Nashville TN, 2003 June.	Abstract
Patrician, P : Army hospitals - Work environment, quality of care, and intent to leave. Army Nurse Corps Chief Nurse Session, AUSA Medical Symposium, San Antonio TX, 2003 June.	Presentation
Patrician, P : The military nursing outcomes database project (MilNOD). Army Nurse Corps Chief Nurse Session, AUSA Medical Symposium, San Antonio TX, 2003 June.	Presentation

## FY 2003 PUBLICATIONS BY DEPARTMENT/SERVICE AND AUTHOR

CITATION	TYPE
Seltzer, C, C Vandrey : Ordinary People, Extraordinary Lives - The Story of Nurses. Sigma Theta Tau, 2003 September.	Publication
Thurmond, V : A study of the relationship between web-based environments and student satisfaction. Second Annual Chesapeake Consortium Research Day - Uncovering the Evidence - Research in Nursing and Health Science, George Mason University, Fairfax VA, 2003 February.	Presentation
Thurmond, V : Assessing the influence of a web-based environment on student satisfaction. Society for Information Technology and Teacher Education International (SITE) Conferences, Albuquerque NM, 2003 March.	Presentation
Thurmond, V : Evaluating the impact of the virtual classroom on students' satisfaction. 13th Annual Summer Institute in Nursing Informatics, Baltimore MD, 2003 July.	Presentation
Thurmond, V : Examination of interaction variables as predictors of students' satisfaction and willingness to enroll in future web-based courses while controlling for student characteristics. Society for Information Technology and Teacher Education International (SITE) Conferences, Albuquerque NM, 2003 March.	Presentation
Thurmond, V : Online environments and student satisfaction (poster). Annual Student Research Forum, Kansas City KS, 2003 April.	Presentation
Thurmond, V : Using hierarchical multiple regression analyses to assess the impact of interactions in web-based course. Annual Student Research Forum, Kansas City KS, 2003 April.	Presentation
Thurmond, V : Assessing the influence of a web-based environment on student satisfaction. Society for Information Technology and Teacher Education International Conference, 2003(1):2518-2525, 2003.	Publication
Thurmond, V : Defining interaction and strategies to enhance interactions in web-based courses. Nurse Educator, 28(5):237-241, 2003.	Publication
Thurmond, V : Examination of interaction variables as predictors of student's satisfaction and willingness to enroll in future web-based courses while controlling for student characteristics. University of Kansas, Parkland FL, <a href="http://www.dissertation.com/library/1121814a.htm">http://www.dissertation.com/library/1121814a.htm</a> , FY03.	Publication
Thurmond, V : Examination of interaction variables as predictors of students' satisfaction and willingness to enroll in future web-based courses while controlling for student characteristics. Society for Information Technology and Teacher Education International Conference, 2003(1):528-531, 2003.	Publication
Thurmond, V, K Wambach, H Connors, B Frey : Evaluation of student satisfaction - Determining the impact of a web-based environment by controlling for student characteristics. The American Journal of Distance Education, 16(3):169-189, 2002 (FY03).	Publication
Thurmond, V, S Popkess-Vawter : Examination of a middle range theory - Applying the input-environment-outcome (I-E-O) model to web-based education. Online Journal of Nursing Informatics, <a href="http://eaa-knowledge.com/ojni/ni/7_2/thurmond.htm">http://eaa-knowledge.com/ojni/ni/7_2/thurmond.htm</a> , 2003.	Publication
Unknown : A study of the safety and feasibility of telenursing for remote cardiac rehabilitation. 8th Annual American Telemedicine Association Meeting, Orlando FL, 2003 April.	Presentation
Unknown : Army Hospitals - Work environment, quality of care, and intent to leave (poster). WRAMC Nurses Week Poster Session, Washington DC, 2003 May.	Presentation
Unknown : Medication error reporting - Anonymous versus formal reporting. 16th Annual Pacific Nursing Research Conference, Honolulu HI, 2003 March.	Presentation
Unknown : Medication error reporting (poster). WRAMC Nurses Week Poster Session, Washington DC, 2003 May.	Presentation

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CITATION	TYPE
Unknown : Medication error reporting and the work environment. 15th Annual Scientific Sessions of the Eastern Nursing Research Society, New Haven CT, 2003 March.	Presentation
Unknown : Medication errors and nurse staffing - What is the connection? (poster). 20th Annual Research Meeting of Academy Health (formerly the Association of Health Services and Policy Research), Nashville TN, 2003 June.	Presentation
Walizer, E : Improving adherence in a Coronary Artery Disease Reversal Program (CADRe) with web-based technology. American Heart Association 2002 Annual Meeting, 2002 November.	Abstract
Walker, J, P Patrician : A study of the safety and feasibility of telenursing for remote cardiac rehabilitation after coronary artery bypass (CABG) surgery (poster). 16th Annual Pacific Nursing Research Conference, Honolulu HI, 2003 March.	Presentation
Winthrop, T, E Vane : Hospitals and terrorism - An operating room perspective. Surgical Services Management Journal, 1:13-16, 2002 (FY03).	Publication
Yoder, L, S Brunken : Peace making/peace keeping missions - Role of the U.S. Army nurse. Critical Care Nursing Clinics of North America, 15(2):265-273, 2003.	Publication

### **DEPARTMENT OF OBSTETRICS AND GYNECOLOGY**

Allard, JE, M Rodriguez, MF Parker : Biopsy site selection at time of colposcopy and distribution of cervical intraepithelial neoplasia: a retrospective chart review. 8th Annual Robert C. Park Research Program, Presentation and Book of Abstracts, Bethesda MD, 2003 May.	Abstract
Allard, JE, NL Carlson, SJ Rogers, J Petrov, MF Parker : A trial of vitamin B complex for the treatment of chemotherapy induced peripheral neuropathy. 41st Meeting of the Armed Forces District of the American College of Obstetricians and Gynecologists, Honolulu HI, 2002 October.	Presentation
Allard, JE, NL Carlson, SJ Rogers, MF Parker, J Petrov : A trial of vitamin B complex for the treatment of chemotherapy induced peripheral neuropathy. 41st Meeting of the Armed Forces District of the American College of Obstetricians and Gynecologists, Presentation and Book of Abstracts, Honolulu HI, 2002 October.	Abstract
Alvero, R, RM Hearn-Stokes, WH Catherino, MP Leondires, JH Segars : The presence of blood or retained embryos in the transfer catheter negatively influences outcome at embryo transfer. Hum Reprod, 18:1848-1852, 2003.	Publication
Armstrong, A, S Dunlow, et al : Predictors of Performance on the Council of Resident Education in Obstetrics & Gynecology (CREOG) Examination (Poster). 2003 CREOG & APOG Annual Meeting, 2003 March.	Presentation
Armstrong, A, S Dunlow, C Nace : Identification, Documentation and Remediation of Problems of Professionalism. Association of Professors of Gynecology and Obstetrics Faculty Development Seminar, 2003 January.	Presentation
Bell, J, M Brady, J Lage, KY Look, N Spirtos, J Walker, GS Rose, YC Young : A Randomized Phase III Trial of Three versus Six Cycles of Carboplatin and Paclitaxel as Adjuvant Treatment in Early Stage Ovarian Epithelial Carcinoma. 34th Annual Meeting of the Society of Gynecologist Oncologists, New Orleans LA, 2003 January.	Abstract
Bell, J, M Brady, J Lage, KY Look, N Spirtos, J Walker, GS Rose, YC Young : A Randomized Phase III Trial of Three versus Six Cycles of Carboplatin and Paclitaxel as Adjuvant Treatment in Early Stage Ovarian Epithelial Carcinoma. 34th Annual Meeting of the Society of Gynecologist Oncologists, New Orleans LA, 2003 January.	Presentation

## FY 2003 PUBLICATIONS BY DEPARTMENT/SERVICE AND AUTHOR

CITATION	TYPE
Blood, B : A Comparison of Techniques in Laparoscopic Appendectomy - Harmonic Scalpel vs. Current Methods. Annual Armed Forces District Meeting of ACOG, Honolulu HI, 2002 October.	Presentation
Blood, B : A Comparison of Techniques in Laparoscopic Appendectomy: Harmonic Scalpel vs. Current Methods. National Capital Consortium, National Naval Medical Center, Washington DC, 2002 October.	Presentation
Blood, B, S Dunlow, E Lockrow : A Comparison of Techniques in Laparoscopic Appendectomy - Harmonic Scalpel vs. Current Methods (Poster). 41st Annual Armed Forces District/American College of Obstetricians and Gynecologists, Honolulu HI, 2002 October.	Presentation
Booth, C, MF Parker, TC Krivak, M Sundborg, J McBroom : Serum and peritoneal analysis in the evaluation of adnexal pathology. Resident Research Day, NNMCMC, WRAMC, 2003 May.	Presentation
Brown, J : Vulvar Cancer in Young Women Infected with the Human Immunodeficiency Virus. USROG Resident Research Day, 2003.	Presentation
Brown, J : Vulvar Cancer in Young Women Infected with the Human Immunodeficiency Virus. American College of Obstetrics and Gynecology Armed Forces District Annual Meeting, 2003.	Presentation
Catherino, WH, C Prupas, JCM Tsibris, PC Leppert, M Payson, LK Nieman, JH Segars : Strategy for elucidating differentially expressed genes in leiomyoma identified by microarray technology. Fertil Steril, 80:282-290, 2003.	Publication
Catherino, WH, JH Segars : Microarray analysis in fibroids - Which list is the correct list?. Fertil Steril, 80:293-294, 2003.	Publication
Dainty, L, GL Maxwell, DL Clarke-Pearson, E Myers : A cost analysis of combination thromboembolism prophylaxis in high risk gynecologic oncology perioperatively. Society of Gynecologic Oncologists, New Orleans LA, 2003.	Abstract
Dainty, LA, WE Winter III, GL Maxwell : The clinical behavior of placental site trophoblastic tumor and contemporary methods of management. Clinical Obstetrics & Gynecology, 46(3):607-611, 2003 September.	Publication
Davis, GD : Gynecologic Urgencies and Emergencies. 38th Parallel Medical Society, Seoul Korea, 2003 April.	Presentation
Davis, GD, A O'Boyle, G Towers, S Seymour, S Russell : Selecting the Appropriate Technique for Vaginal Hysterectomy. J Pelvic Med Surg, 2(2):241-244, 2003 April.	Publication
Davis, GD, A Towers, A O'Boyle : Selecting the Appropriate Technique for Vaginal Hysterectomy. Annual Armed Forces District Meeting of ACOG, Honolulu HI, 2002 October.	Presentation
Davis, GD, A Towers, A O'Boyle : Teaching the Evaluation and Repair of Obstetrical Lacerations with the Beef Tongue Model. Annual Armed Forces District Meeting of ACOG, Honolulu HI, 2002 October.	Presentation
Davis, GD, A Towers, A O'Boyle : The Various Mechanisms of Paravaginal Defects Occurring Among Female Soldiers. Annual Armed Forces District Meeting of ACOG, Honolulu HI, 2002 October.	Presentation
Deering, SH, J Heller, C Winkel, HJ Landy : Intrauterine head entrapment of a second twin by uterine synechiae. Obstetrics & Gynecology, 104:693-695, 2003.	Publication
Dunlow, SG : Trauma in Pregnancy. Grand Rounds, Bethesda Navy Medical Center, Department of Obstetrics and Gynecology, Bethesda MD, 2003 September.	Presentation
Elkas, JC, CH Holschneider, B Katz, AJ Li, R Louie, KF McGonigle, JS Berek : The use of continuous infusion topotecan in persistent and recurrent ovarian cancer. Int J Gynecol Cancer, 13(2):138-141, 2003.	Publication

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CITATION	TYPE
Farley, JH, K Hickey, JW Carlson, GS Rose, KE Kost, TA Harrison : Adenosquamous Histology Predicts Poor Outcome for Advanced but Not Early Stage Cervical Adenocarcinomas (Poster and Book of Abstracts). 34th Annual Meeting of the Society of Gynecologic Oncologists, New Orleans LA, 2003 January.	Abstract
Farley, JH, KW Hickey, JW Carlson, GS Rose, ER Kost, TA Harrison : Adenosquamous histology predicts a poor outcome for patients with advanced stage but not early stage cervical carcinoma. Cancer, 97(9):2196-2202, 2003 May.	Publication
Frattarelli, JL, AJ Levi, BT Miller, JH Segars : A prospective assessment of the predictive value of basal antral follicles in in vitro fertilization cycles. Fertil Steril, 80:350-355, 2003.	Publication
Green : Title not available. SGO, 2003.	Abstract
Jones, M, T Greenwood, A Berchuck, GL Maxwell, K Podratz : Localization and Clinicopathological Correlations of GEP Expression in Endometrial Carcinomas. SGO 2003, New Orleans LA, 2003.	Abstract
Kost, ER, KL Hall, JF Hines, JH Farley, LR Nycum, GS Rose, JW Carlson, JR Fischer Jr., BS Kendall : Asian-Pacific Islander race independently predicts poor outcome in patients with endometrial cancer. Gynecol Oncol, 89(2):218-226, 2003 May.	Publication
Krishnan, A, C Murdoch, J Allard, M Cisar, E Reid, L Nieman, J Segars : Pseudo-isolated FSH deficiency caused by an inhibin B secreting granulosa cell tumor - case report. Human Reproduction, 18(3):502-505, 2003.	Publication
Larsen, FW, GM Couchman, DK Walmer : Acute renal failure due to bilateral ureteral compression following in vitro fertilization - Embryo transfer - A case report (poster). Annual Meeting of the Armed Forces District of the American College of Obstetricians and Gynecologists, Honolulu HI, 2002 October.	Presentation
Luterzo, J, J Parker, A Armstrong, R Alvero : A curriculum and performance assessment tool for saline sonohysterography. Annual Meeting of the American Society of Reproductive Medicine, San Antonio TX, 2003.	Presentation
Maxwell, GL, JW Carlson, M Ochoa, T Krivak, GS Rose, ER Myers : Costs and effectiveness of alternative strategies for cervical cancer screening in military beneficiaries. Obstet Gynecol, 100(4):740-748, 2002 October.	Publication
Mayers, KS, JA Heller : Sexuality and the late stage Huntington's Disease patient. Sexuality and Disability, 21(2):91-105, 2003.	Publication
Miller, C, JW McBroom, GS Rose, A Yemelyanova, J Cosin : Malignant transformation of a benign cystic teratoma into a pancreatic type endocrine neoplasm (Presentation and Book of Abstracts). 6th Annual Robert C. Park Resident Research Program, Bethesda MD, 2003 May.	Presentation
O'Boyle, A, GD Davis, B Calhoun : Informed consent and birth - Protecting the pelvic floor and ourselves. Am J Obstet Gynecol, 187(4):981-993, 2002 November.	Publication
Parker, J, J Broberg, P Napolitano : Arnold Chiari-Malformation - A Labor Management Dilemma. Am J Perinatology, 19(8):445-449, 2002 (FY03).	Publication
Parker, J, J O'Boyle : Massive hydrothorax following a granulosa cell tumor. APGO/CREOG Meeting, Anaheim CA, 2003.	Presentation
Parker, J, J Segars, J McKeeby : Does assisted hatching improve pregnancy rates in women under the age of 40?. ACOG Armed Forces District Meeting, San Antonio TX, 2003.	Presentation
Parker, J, J Segars, J McKeeby : Prolonged ovarian suppression with OCPs. ACOG Armed Forces District Meeting, San Antonio TX, 2003.	Presentation



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CITATION	TYPE
Parker, J, M Leondires, J Segars, J McKeeby : Ovarian suppression with oral contraceptive pills prior to ART - Can you get too much of a good thing?. Annual Meeting of the American Society of Reproductive Medicine, San Antonio TX, 2003.	Presentation
Parker, J, R Alvero, A Armstron : Teaching residents how to perform saline sonohysterography. ACOG Armed Forces District Meeting, San Antonio TX, 2003.	Presentation
Preen, AE, JL McKeeby, W Catherino, RJ Alvero : Oral misoprostol prior to operative hysteroscopy does not enhance cervical dilation or improve operative time - A prospective, randomized, double-blind, placebo-controlled trial. 58th Annual Meeting of the American Society for Reproductive Medicine, Seattle WA, 2002 October.	Presentation
Risinger, J, GL Maxwell, B Davis, C Zahn, A Berchuck, JC Barrett : Promoter hypermethylation as an epigenetic component in Type I and Type II endometrial cancers. Ann NY Acad Sci, 983:208-212, 2003.	Publication
Risinger, J, GL Maxwell, G Chandramouli, A Jazaeri, O Aprelikova, T Patterson, C Barrett, A Berchuck : Microarray analysis reveals distinct expression profiles among different histologic types of endometrial cancer. Cancer Research, 63:6-11, 2003.	Publication
Risinger, J, GL Maxwell, G Chandramouli, A Jazaeri, O Sprelikova, T Patterson, C Barrett, A Berchuck : Microarray expression profiles in endometrial cancer. SGO 2003, New Orleans LA, 2003.	Abstract
Robinson, NL, M Wilhelm, J Sunde, W Winter, GS Rose : Hypersensitivity to Paclitaxel, Docetaxel and Liposomal Doxorubicin in a Patient with Advanced Ovarian Cancer. 6th Annual Robert C. Park Resident Research Program, Bethesda MD, 2003 May.	Abstract
Robinson, NL, M Wilhelm, J Sunde, W Winter, GS Rose : Hypersensitivity to Paclitaxel, Docetaxel and Liposomal Doxorubicin in a Patient with Advanced Ovarian Cancer (Presentation and Book of Abstracts). 6th Annual Robert C. Park Resident Research Program, Bethesda MD, 2003 May.	Abstract
Robinson, NL, M Wilhelm, J Sunde, W Winter, GS Rose : Hypersensitivity to Paclitaxel, Docetaxel and Liposomal Doxorubicin in a Patient with Advanced Ovarian Cancer. 6th Annual Robert C. Park Resident Research Program, Bethesda MD, 2003 May.	Presentation
Stany, MP, JL Buller : Sacral Neuromodulation - Applications in the management of complex pelvic floor dysfunction. 6th Annual Robert C. Park Resident Research Program, Bethesda MD, 2003 May.	Abstract
Stany, MP, JL Buller : Sacral Neuromodulation - Applications in the management of complex pelvic floor dysfunction. 6th Annual Robert C. Park Resident Research Program, Bethesda MD, 2003 May.	Presentation
Tejada-Berges, T, R Binder, PK Srivastava, GS Rose : Evaluating the Efficacy of Therapeutic Vaccination with Tumor-Derived gp96 Peptide Complexes Using a Syngeneic Rat Model of Ovarian Cancer (Poster and Book of Abstracts). 34th Annual Meeting of the Society of Gynecologic Oncologists, New Orleans LA, 2003 January.	Abstract
Tejada-Berges, T, R Binder, PK Srivastava, GS Rose : In Vitro Synergism between Paclitaxel and the Farnesyl Transferase Inhibitor FTI-277 in Epithelial Ovarian Carcinoma Cell Lines (Poster and Book of Abstracts). 34th Annual Meeting of the Society of Gynecologic Oncologists, New Orleans LA, 2003 January.	Abstract
Trimble, C : Reproducibility of the Diagnosis of Atypical Endometrial Hyperplasia (A Gynecologic Oncology Group Study). SGO 34th Annual Meeting, 58, 2003 January-February.	Abstract
Tsibris, JCM, J Segars, S Enkemann, D Coppola, G Wilbanks, WF O'Brien, WN Spellacy : New and old regulators of uterine leiomyoma growth from screening with cDNA arrays. Fertil Steril, 80:279-281, 2003.	Publication

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CITATION	TYPE
Webb, JC, H Donninger, VD Leaner, GS Rose, JW Carlson, JH Farley, MJ Birrer : Effect of Cyclin E Overexpression on Human Ovarian Carcinoma Cell Lines In Vitro (Poster and Book of Abstracts). 34th Annual Meeting of the Society of Gynecologic Oncologists, New Orleans LA, 2003 January.	Abstract
Webb, JC, H Donninger, VD Leaner, GS Rose, JW Carlson, JH Farley, MJ Birrer : Effect of Cyclin E Overexpression on Human Ovarian Carcinoma Cell Lines In Vitro (Poster and Book of Abstracts). 34th Annual Meeting of the Society of Gynecologic Oncologists, New Orleans LA, 2003 January.	Abstract
Webb, JC, H Donninger, VD Leaner, GS Rose, JW Carlson, JH Farley, MJ Birrer : Evaluating the Efficacy of Therapeutic Vaccination with Tumor-Derived gp96 Peptide Complexes Using a Syngeneic Rat Model of Ovarian Cancer (Poster and Book of Abstracts). 34th Annual Meeting of the Society of Gynecologic Oncologists, New Orleans LA, 2003 January.	Abstract
William, WE, PR Kucera, W Rodgers, JW McBroom, C Olsen, LC Maxwell : Surgical staging in patients with ovarian tumors of low malignant potential. Obst Gynecol, 100(4):671-676, 2002 October.	Publication
Winter, W, GS Rose, LA Padilla, CR Key, CR Qualls, HO Smith : Mortality and Second Primary Malignancies in Early Invasive Cervix Cancer (Poster and Book of Abstracts). 34th Annual Meeting of the Society of Gynecologic Oncologists, New Orleans LA, 2003 January.	Abstract
Winter, W, GS Rose, LA Padilla, CR Key, CR Qualls, HO Smith : Mortality and Second Primary Malignancies in Early Invasive Cervix Cancer (Poster and Book of Abstracts). 34th Annual Meeting of the Society of Gynecologic Oncologists, New Orleans LA, 2003 January.	Abstract
Winter, W, J Seidman, T Krivak, S Chauhan, JW Carlson, GS Rose, MJ Birrer : Clinicopathological Analysis of c-kit Expression in Sarcomas of the Uterine Corpus (Poster and Book of Abstracts). 34th Annual Meeting of the Society of Gynecologic Oncologists, New Orleans LA, 2003 January.	Abstract
Winter, W, J Seidman, T Krivak, S Chauhan, JW Carlson, GS Rose, MJ Birrer : Clinicopathological Analysis of c-kit Expression in Sarcomas of the Uterine Corpus (Poster and Book of Abstracts). 34th Annual Meeting of the Society of Gynecologic Oncologists, New Orleans LA, 2003 January.	Abstract
Winter, WE III, MW McBroom, JW Carlson, SG ose, JC Elkas : The utility of gastrojejunostomy in secondary cytoreduction and palliation of proximal intestinal obstruction in recurrent ovarian cancer. Gyn Onc, 91(1):261-264, 2003.	Publication
Wright, TC, JT Cox, LS Massad, J Carlson, LB Twiggs, EJ Wilkinson : ASCCP-sponsored Consensus Workshop 2001 Consensus guidelines for the management of women with cervical intraepithelial neoplasia. J Lower Genital Tract Dis, 5:154-167, 2003 July.	Publication
Wright, TC Jr., JT Cox, LS Massad, J Carlson, LB Twiggs, EJ Wilkinson : American Society for Colposcopy and Cervical Pathology 2001 consensus guidelines for the management of women with cervical intraepithelial neoplasia. Am J Obstet Gynecol, 189(1):295-304, 2003 July.	Publication

### **DEPARTMENT OF ORTHOPAEDIC SURGERY AND REHABILITATION**

#### **Occupational Therapy Service**

Amaker, R : Upper extremity splinting - Nerve injuries in the war casualty (poster). Medical Association of the United States Army (AUSA) Meeting, San Antonio TX, 2003 June.	Presentation
Amaker, R, R Bannon, A Burke, L Stawarczik, M Tenhor : Pain perceptions and adaptations among Walter Reed Army Medical Center Beneficiaries (poster). American Occupational Therapy Association (AOTA) Annual Conference, Washington DC, 2003 June.	Presentation
Amaker, R, R Bannon, A Burke, L Stawarczik, M Tenhor : Pain perceptions and adaptations among Walter Reed Army Medical Center Beneficiaries Seminar. American Occupational Therapy Association (AOTA) Annual Conference, Washington DC, 2003 June.	Presentation

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CITATION	TYPE
<b><u>Orthopaedic Surgery Service</u></b>	
: Evaluation of orthopaedic injuries in Operation Enduring Freedom. Society of Military Orthopaedic Surgeons Annual Meeting, San Diego CA, 2002 December.	Presentation
: Functional outcomes following arthroscopically assisted combined anterior and posterior cruciate ligament reconstruction in a physically active population. Society of Military Orthopaedic Surgeons, San Diego CA, 2002 December.	Presentation
: Probing for thoracic pedicle screw tract violation(s) - Is it valid?. Society of Military Orthopaedic Surgeons, San Diego CA, 2002 December.	Presentation
: Subtalar dislocation in an 8-year-old male (poster). 44th Annual Meeting of the Society of Military Orthopaedic Surgeons, San Diego CA, 2002 December.	Presentation
: The radioscapoid interval - A sensitive indicator of early perilunar instability?. Society of Military Orthopaedic Surgeons, San Diego CA, 2002 December.	Presentation
Belmont, P, K Taylor, T Kuklo, J Prahinski, R Kruse : Occult intraspinal anomalies in association with an isolated congenital hemivertebra - The role of routine magnetic resonance imaging. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Belmont, PJ, KF Taylor, TR Kuklo, JR Prahinski, RW Kruse : Occult intraspinal anomalies in association with an isolated congenital hemivertebra - The role of routine magnetic resonance imaging. Society of Military Orthopaedic Surgeons 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Bojescul, JA, JS Xenos, JJ Callaghan, CG Savory : Results of porous-coated anatomic total hip arthroplasty without cement at fifteen years: a concise follow-up of a previous report. J Bone Joint Surg Am, 85-A(6):1079-1083, 2003 June.	Publication
Cooper, P, S Shawen et al : Fine wire external fixation for the management of chronic ulcerations associated with charcot arthropathy. Society of Military Orthopaedic Surgeons, San Diego CA, 2002 December.	Presentation
Cooper, P, S Shawen et al : Fine wire external fixation for the management of chronic ulcerations associated with charcot arthropathy. American Academy of Orthopaedic Surgeons, New Orleans LA, 2003.	Presentation
Dhawan, A, A Ross, S Rose, M Lenhart, F Farber : Revision ulnar nerve decompression. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Dhawan, A, W Doukas : Acute compartment syndrome of the foot following an inversion injury to the ankle with anterior tibial artery disruption. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Dhawan, A, W Klemme, B Runyon, D Polly : Thoracic pedicle screws - Comparison of start points and trajectories. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Dinauer, P, JA Bojescul, KJ Kaplan, Litts : Bilateral lipoma arborescens of the bicipitoradial bursa. Skeletal Radiol, 31(11):661-665, 2002 November.	Publication
Freedman, B, K Taylor : The radioscapoid interval - A sensitive indicator of early perilunar instability (poster). 34th Meeting of the Society of Military Orthopaedic Surgeons, San Diego CA, 2002 December.	Presentation
Freedman, B, K Taylor, C Litts, G Farber : The radioscapoid interval - A poor indicator of early scapholunate instability. 44th Annual Meeting of the Society of Military Orthopaedic Surgeons, San Diego CA, 2002 December.	Presentation

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CITATION	TYPE
Freedman, B, S Cohen, T Kuklo, J Giuliani, R Lehman, P Larkin : Intradiscal electrothermal therapy for chronic low back pain in active duty soldiers. 44th Annual Meeting of the Society of Military Orthopaedic Surgeons, San Diego CA, 2002 December.	Presentation
Freedman, B, S Cohen, T Larkin, R Lehman, T Kuklo : Intradiscal electrothermography for chronic low back pain in active duty soldiers. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Freedman, BA, SR Cohen, TM Larkin, RA Lehman, J Guliani, TR Kuklo : Intradiscal electrothermography for chronic low back pain in active duty soldiers. Society of Military Orthopaedic Surgeons 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Gajewski, DA, JB Burnette, MD Murphey, HT Temple : Differentiating clinical and radiographic features of enchondroma versus secondary chondrosarcoma in the foot. American Academy of Orthopaedic Surgeons 70th Annual Meeting, New Orleans LA, 2003 February.	Presentation
Graham, E, TR Kuklo, R Kyriakos, P Rubin, KD Riew : Pigmented villonodular synovitis of the atlantoaxial joint. J Bone Joint Surg, 84(A):1856-1860, 2002 October.	Publication
Groth, A, W Klemme, D Polly, T Kuklo, Schroeder : Comparison of sagittal contour and posterior disc height following interbody fusion - Threaded cages versus structural allograft versus vertical cages. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Groth, AG, TR Kuklo, WR Klemme, DW Polly, TM Schroeder : Comparison of sagittal contour and posterior disk height following interbody fusion - Threaded cylinder cages versus structural allograft versus vertical cages. 10th International Meeting on Advanced Spine Techniques (IMAST), Rome Italy, 2003 July.	Presentation
Groth, AT, WR Klemme, DW Polly, TR Kuklo, TM Schroeder : Comparison of sagittal contour and posterior disc height following interbody fusion - Threaded cages versus structural allograft versus vertical cages. Society of Military Orthopaedic Surgeons 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Javernick, MA, TR Kuklo, DW Polly Jr., TM Schroeder : Transforaminal lumbar interbody fusion - Unilateral vs. bilateral disc removal - an in vivo study. 44th Annual Meeting of the Society of Military Orthopaedic Surgery, San Diego CA, 2002 December.	Presentation
Kirk, K, TR Kuklo, DW Polly : Assessment of the proximal thoracic curve with traction versus slide-bending radiographs. Am J Orthop, 32(6):284-288, 2003.	Publication
Kirk, KL, JS Xenos, RA Lehman, LD Topeleski, R Howard : The effect of distal stem design on interface motion in revision femoral stems. WRAMC Orthopedic Research Day, Washington DC, FY not submitted.	Presentation
Kirk, KL, JS Xenos, RA Lehman, O Vesnosky, LD Topeleski, R Howard : The effect of distal stem geometry on interface motion in uncemented revision total hip prostheses. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Kirk, KL, KA McHale, M Lenhart : Outcomes of cuboid/cuneiform osteotomies for the treatment of the "bean-shaped" foot. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Kuklo, T, R Lehman : The effect of tapping versus untapping before placement of thoracic pedicle screws - A biomechanical study. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Kuklo, T, R Lehman, L Lenke : Preoperative and postoperative CT evaluation of structures at risk with anterior spinal fusion. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation

## FY 2003 PUBLICATIONS BY DEPARTMENT/SERVICE AND AUTHOR

CITATION	TYPE
Kuklo, TR : A biomechanical analysis of tapping versus untapping the thoracic pedicle screw tract. Chirurgien des Hôpitaux de Paris, Hôpital Saint Vincent de Paul, Paris France, 2003 June.	Presentation
Kuklo, TR : A biomechanical analysis of tapping versus untapping the thoracic pedicle screw tract. University of Nottingham, Queen's Medical Centre, Centre of Spinal Studies and Surgery, Nottingham England, 2003 July.	Presentation
Kuklo, TR : A biomechanical analysis of tapping versus untapping the thoracic pedicle screw tract. Florence Nightingale Hospital, Istanbul Spine Center, Istanbul Turkey, 2003 June.	Presentation
Kuklo, TR : A biomechanical analysis of tapping versus untapping the thoracic pedicle screw tract. Calot Institute, Service du Chirurgie Orthopédique, Berck Sur Mer France, 2003 June.	Presentation
Kuklo, TR : Accuracy and efficacy of thoracic pedicle screws in curves over 90 degrees. University of Athens School of Medicine, KAT Accident Hospital, Athens Greece, 2003 June.	Presentation
Kuklo, TR : Accuracy and efficacy of thoracic pedicle screws in curves over 90 degrees. University of Nottingham, Queen's Medical Centre, Centre of Spinal Studies and Surgery, Nottingham England, 2003 July.	Presentation
Kuklo, TR : Biomechanical analysis of tapping versus untapping the thoracic pedicle screw tract. University of Athens School of Medicine, KAT Accident Hospital, Athens Greece, 2003 June.	Presentation
Kuklo, TR : Correlation of shoulder height and balance with radiographs for adolescent idiopathic scoliosis - Clinical decision making. University of Athens School of Medicine, KAT Accident Hospital, Athens Greece, 2003 June.	Presentation
Kuklo, TR : Correlation of shoulder height and balance with radiographs for adolescent idiopathic scoliosis - Clinical decision making. Florence Nightingale Hospital, Istanbul Spine Center, Istanbul Turkey, 2003 June.	Presentation
Kuklo, TR : Effect of alendronate sodium on spinal fusion - A rabbit model. Florence Nightingale Hospital, Istanbul Spine Center, Istanbul Turkey, 2003 June.	Presentation
Kuklo, TR : Finite element modeling of thoracic pedicle screw constructs. Klinikum Neustadt, Center for Spine Surgery and Scoliosis, Neustadt Germany, 2003 June.	Presentation
Kuklo, TR : Hemimetameric Shift. University of Athens School of Medicine, KAT Accident Hospital, Athens Greece, 2003 June.	Presentation
Kuklo, TR : Image acquisition validation of a scoliosis model. Centre des Massues, Lyon France, 2003 June.	Presentation
Kuklo, TR : Intradiscal electrothermal therapy for chronic low back pain - Minimum 24-month follow-up. Klinikum Neustadt, Center for Spine Surgery and Scoliosis, Neustadt Germany, 2003 June.	Presentation
Kuklo, TR : Isolated hemivertebra - Associated intraspinal anomalies. University of Athens School of Medicine, KAT Accident Hospital, Athens Greece, 2003 June.	Presentation
Kuklo, TR : Reliability of digital radiographic measurements for scoliosis evaluation. Centre des Massues, Lyon France, 2003 June.	Presentation
Kuklo, TR : Sagittal trajectory change for salvage of failed thoracic pedicle screws. Calot Institute, Service du Chirurgie Orthopédique, Berck Sur Mer France, 2003 June.	Presentation
Kuklo, TR : Sagittal trajectory change for salvage of failed thoracic pedicle screws. University of Athens School of Medicine, KAT Accident Hospital, Athens Greece, 2003 June.	Presentation

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CITATION	TYPE
Kuklo, TR : Sagittal trajectory change for salvage of failed thoracic pedicle screws. University of Nottingham, Queen's Medical Centre, Centre of Spinal Studies and Surgery, Nottingham England, 2003 July.	Presentation
Kuklo, TR : Sagittal trajectory change for salvage of failed thoracic pedicle screws. Chirurgien des Hospitaux de Paris, Hospital Saint Vincent de Paul, Paris France, 2003 June.	Presentation
Kuklo, TR : Sagittal trajectory change for salvage of failed thoracic pedicle screws. Florence Nightingale Hospital, Istanbul Spine Center, Istanbul Turkey, 2003 June.	Presentation
Kuklo, TR : Sagittal versus coronal trajectory - A biomechanical evaluation. Florence Nightingale Hospital, Istanbul Spine Center, Istanbul Turkey, 2003 June.	Presentation
Kuklo, TR : Sagittal versus coronal trajectory - A biomechanical evaluation. University of Nottingham, Queen's Medical Centre, Centre of Spinal Studies and Surgery, Nottingham England, 2003 July.	Presentation
Kuklo, TR : Sagittal versus coronal trajectory - A biomechanical evaluation. University of Athens School of Medicine, KAT Accident Hospital, Athens Greece, 2003 June.	Presentation
Kuklo, TR : Sagittal versus coronal trajectory for thoracic pedicle screws - A biomechanical evaluation. Calot Institute, Service du Chirurgie Orthopedique, Berck Sur Mer France, 2003 June.	Presentation
Kuklo, TR : Sagittal versus coronal trajectory for thoracic pedicle screws - A biomechanical evaluation. Chirurgien des Hospitaux de Paris, Hospital Saint Vincent de Paul, Paris France, 2003 June.	Presentation
Kuklo, TR : Screws in curves over 90 degrees. Florence Nightingale Hospital, Istanbul Spine Center, Istanbul Turkey, 2003 June.	Presentation
Kuklo, TR : Spontaneous proximal thoracic curve correction in AIS. Florence Nightingale Hospital, Istanbul Spine Center, Istanbul Turkey, 2003 June.	Presentation
Kuklo, TR : Spontaneous proximal thoracic curve correction in AIS. University of Athens School of Medicine, KAT Accident Hospital, Athens Greece, 2003 June.	Presentation
Kuklo, TR : Thoracic screw biomechanics. Chirurgien des Hospitaux de Paris, Hospital Saint Vincent de Paul, Paris France, 2003 June.	Presentation
Kuklo, TR, BD Owens, DW Polly : Peri-operative blood and blood product management for spinal deformity. The Spine Journal, 3(4):1-6, 2003.	Publication
Kuklo, TR, MF O'Brien, K Altobelli, TS Schroeder : Reliability of digital radiographic measurements for scoliosis evaluation. 10th International Meeting on Advanced Spine Techniques (IMAST), Rome Italy, 2003 July.	Presentation
Kuklo, TR, RA Lehman : Effect of tapping versus untapping before placement of thoracic pedicle screws - A biomechanical analysis. Society of Military Orthopaedic Surgeons 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Kuklo, TR, RA Lehman : Effect of tapping versus untapping before placement of thoracic pedicle screws - A biomechanical analysis. Spine, 28(18):2066-2071, 2003.	Publication
Kuklo, TR, RA Lehman, BA Freedman, J Coward, KD Riew : The effect of alendronate sodium on spinal fusion - A rabbit model. 10th International Meeting on Advanced Spine Techniques (IMAST), Rome Italy, 2003 July.	Presentation
Kuklo, TR, RA Lehman, LG Lenke : Preoperative and postoperative computer tomography evaluation of structures at risk with anterior spinal fusion (poster). NASS 17th Annual Meeting, 2002 October.	Presentation

## FY 2003 PUBLICATIONS BY DEPARTMENT/SERVICE AND AUTHOR

CITATION	TYPE
Kuklo, TR, RA Lehman, LG Lenke : Preoperative and postoperative CT evaluation of structures at risk with ASF. Eastern and Southern Orthopaedic Association Annual Meeting, Dublin Ireland, 2003 July-August.	Presentation
Kuklo, TR, RA Lehman, LG Lenke : Preoperative and postoperative CT evaluation of structures at risk with ASF. World Spine II, Chicago IL, 2003 August.	Presentation
Kuklo, TR, RA Lehman, LG Lenke : Preoperative and postoperative CT evaluation of structures at risk with ASF. World Spine II, Chicago IL, 2003 August.	Presentation
Kuklo, TR, RA Lehman, LG Lenke : Preoperative and postoperative CT evaluation of structures at risk with ASF. Society of Military Orthopaedic Surgeons 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Kuklo, TR, RA Lehman, LG Lenke : Preoperative and postoperative CT evaluation of structures at risk with ASF. American Academy of Orthopaedic Surgeons 70th Annual Meeting, New Orleans LA, 2003 February.	Presentation
Kuklo, TR, TS Schroeder : Comparison of digital radiographic measurements with varying resolution. 10th International Meeting on Advanced Spine Techniques (IMAST), Rome Italy, 2003 July.	Presentation
Lehman, R, T Kuklo, B Freedman, D Riew : The effect of alendronate sodium on spinal fusion in a rabbit model. 44th Annual Meeting of the Society of Military Orthopaedic Surgeons, San Diego CA, 2002 December.	Presentation
Lehman, RA, D Polly, T Kuklo, B Cunningham, K Kirk, P Belmont : Advantage of straight-forward versus anatomic trajectory for placement of thoracic pedicle screws - A biomechanical analysis. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Lehman, RA, DW Polly, TR Kuklo, BW Cunningham, KL Kirk, PJ Belmont : Advantage of straight-forward versus anatomic trajectory of thoracic pedicle screws - A biomechanical model. Washington Orthopaedic Society Resident Competition, Washington DC, 2003 May.	Presentation
Lehman, RA, DW Polly, TR Kuklo, BW Cunningham, KL Kirk, PJ Belmont : Advantage of straight-forward versus anatomic trajectory of thoracic pedicle screws - A biomechanical model. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Lehman, RA, DW Polly, TR Kuklo, BW Cunningham, KL Kirk, PJ Belmont : Advantage of straight-forward versus anatomic trajectory of thoracic pedicle screws - A biomechanical model. World Spine II, Chicago IL, 2003 August.	Presentation
Lehman, RA, DW Polly, TR Kuklo, BW Cunningham, KL Kirk, PJ Belmont : Straight-forward versus anatomic trajectory of thoracic pedicle screws. Eastern and Southern Orthopaedic Association Annual Meeting, Dublin Ireland, 2003 July-August.	Presentation
Lehman, RA, DW Polly, TR Kuklo, BW Cunningham, KL Kirk, PJ Belmont : Straight-forward versus anatomic trajectory of thoracic pedicle screws - A biomechanical analysis. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Lehman, RA, DW Polly, TR Kuklo, BW Cunningham, KL Kirk, PJ Belmont : Straight-forward versus anatomic trajectory of thoracic pedicle screws - A biomechanical analysis. 9th International Meeting of Advanced Spine Techniques, San Diego, CA, 2002 December.	Presentation
Lehman, RA, DW Polly, TR Kuklo, BW Cunningham, KL Kirk, PJ Belmont : Straight-forward versus anatomic trajectory for thoracic pedicle screws - A biomechanical study. Spine, 28(18):2058-2065, 2003.	Publication
Lehman, RA, KP Potter, TR Kuklo, JO Orchowski, DW Polly, AS Chang : Pedicle probing for detection of thoracic pedicle screw violation(s) - Is it valid?. Eastern Orthopaedic Association/Southern Orthopaedic Association Annual Meeting, Dublin Ireland, 2003 July-August.	Presentation

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CITATION	TYPE
Lehman, RA, TR Kuklo : Use of anatomic trajectory for thoracic pedicle screw salvage after failure/violation using the straight-forward technique - A biomechanical analysis. Spine, 28(18):2072-2077, 2003.	Publication
Lehman, RA, TR Kuklo, BA Freedman, J Coward, KD Riew : The effect of alendronate sodium on spinal fusion - A rabbit model. Washington Orthopaedic Society Resident Competition, Washington DC, 2003 May.	Presentation
Lehman, RA, TR Kuklo, BR Freedman, J Cowart, KD Riew : The effect of alendronate sodium on spinal fusion - A rabbit model. Washington Orthopaedic Society, Washington DC, 2003 May.	Presentation
Lenhart, M, L Smurr, J Clasing, R Amaker, G Bogumill : The history of upper extremity splinting. Eastern Ortho. Association, Amelia Island FL, 2002 October.	Presentation
Lenhart, M, L Smurr, J Clasing, R Amaker, G Bogumill : The history of upper extremity splinting. American Society for Surgery of the Hand, Phoenix AZ, 2002 October.	Presentation
Lin, DL, KL Kirk, KP Murphy, KA McHale, WC Doukas : Evaluation of orthopaedic injuries in Operation Enduring Freedom. Mil Med, 2003.	Publication
Lin, DL, KL Kirk, KP Murphy, WC Doukas, KA McHale : Evaluation of orthopaedic injuries from Operation Enduring Freedom. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Lin, DL, KL Kirk, KP Murphy, WC Doukas, KA McHale : Evaluation of Orthopaedic Injuries in Operation Enduring Freedom. Society of Military Orthopaedic Surgeons 42nd Annual Meeting, San Diego CA, 2002 December.	Presentation
Long, J, SJ Lewis, TR Kuklo, Y Zhu, KD Riew : The effect of Cox-2 inhibitors on spinal fusion. J Bone Joint Surg, 84(A):1763-1768, 2002 October.	Publication
Machen, MS, JE Tis, N Inoue, RH Meffert, EY Chao, KA McHale : The effect of low intensity pulsed ultrasound on regenerate bone in a less-than-rigid biomechanical environment. Biomed Mater Eng, 12(3):239-247, 2002 (FY03).	Publication
McHale, K, A Ross : Keystone fusion for chronic Lisfranc's fracture-dislocation. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
McHale, KA, PJ Pollock, C McHale : Ballistics and Wounding - An overview of the mechanics and treatment. Society of Military Orthopaedic Surgeons Annual Meeting, San Diego CA, 2002 December.	Presentation
Murphy, K, K Taylor, K Kirk, P Belmont, S Shawen, W Doukas : Functional outcomes following arthroscopically assisted combined anterior and posterior cruciate ligament reconstruction. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Murphy, KP : Arthroscopic treatment of lateral epicondylitis. AANA Fall Course, Palm Desert CA, 2002 November.	Presentation
Murphy, KP : Multiligament knee reconstruction in a high demand population. Fifth Annual Omer Orthopaedic Seminar, San Antonio TX, 2003 April.	Presentation
Murphy, KP : Multiligament reconstruction of the knee - 2-Year retrospective results. SOMOS Annual Meeting, San Diego CA, 2002 December.	Presentation
Nicholson, J, RE Wallace, M Myerson : Micromotion and contact pressure of the agility total ankle with and without a subtalar fusion. WRAMC DOS&R Research Day, 2003 June.	Presentation



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CITATION	TYPE
O'Brien, MF, TR Kuklo, BS Richards, LG Lenke, DW Polly, D Schreiber, R Pinteric, TS Schroeder, KM Blanke : A multicenter clinical and radiographic analysis of anterior and posterior surgical techniques for treatment of thoracolumbar/lumbar AIS - The current state of the art. Scoliosis Research Society 38th Annual Meeting, Quebec City Canada, 2003 September.	Presentation
Polly, DW, BW Cunningham, TR Kuklo, LG Lenke, I Ota, TM Schroeder, WR Klemme : Anterior thoracic scoliosis constructs - Effect of rod diameter and intervertebral cages on multi-segmental construct stability. The Spine Journal, 3(3):213-219, 2003.	Publication
Polly, DW, T Kuklo, M O'Brien, T Schroeder, L Nelson, L Lenke : Reliability of radiographic parameters for scoliosis evaluation. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Polly, DW, TR Kuklo : Iliac crest bone graft pain. World Spine II, Chicago IL, 2003 August.	Presentation
Polly, DW, TR Kuklo, MF O'Brien, TM Schroeder, L Nelson, LG Lenke : Reliability of radiographic parameters for scoliosis evaluation. Society of Military Orthopaedic Surgeons 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Polly, DW, TR Kuklo, T Schroeder, T Boal : Telemedicine Screening of Adolescent Idiopathic Scoliosis. 8th Annual American Telemedicine Conference, Orlando FL, 2003 April.	Presentation
Potter, BK, RA Lehman, WC Doukas : Simultaneous bilateral pectoralis major tendon ruptures - Case report and review of literature. J Bone Joint Surg, 2003.	Publication
Rosner, M, DW Polly, TR Kuklo, S Ondra : Thoracic pedicle screw fixation for spinal deformity. Neurosurgical Focus - J of Neurosurgery, 14(1):1-6, 2003.	Publication
Shawen, S, R Lehman, T Kuklo, J Orchowski, B Potter, A Chang, D Polly : Probing for thoracic pedicle screw tract violation. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Shawen, SB, PJ Belmont Jr., TR Kuklo, BD Owens, KF Taylor, R Kruse, DW Polly Jr. : Hemimetameric segmental shift - A case series and review. Spine, 27(24):E539-544, 2002 December.	Publication
Shawen, SB, PJ Belmont Jr., WR Klemme, LD Topoleski, JS Xenos, JR Orchowski : Osteoporosis and anterior femoral notching in periprosthetic supracondylar femoral fractures - A biomechanical analysis. J Bone Joint Surg Am, 85-A(1):115-121, 2003 January.	Publication
Shawen, SB, RA Lehman, TR Kuklo, JO Orchowski, KP Potter, AS Chang, DW Polly : Probing for thoracic pedicle screw tract violation(s) - Is it valid?. Society of Military Orthopaedic Surgeons 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Taylor, K, B Rafiee, N Inoue, J Tis, K McHale, E Chao : The effect of pulsed electromagnetic fields on maturation of regenerate bone in rabbit limb lengthening model. Society of Military Orthopaedic Surgeons (SOMOS) 44th Annual Meeting, San Diego CA, 2002 December.	Presentation
Temple, HT, A Mollabashy, DA Gajewski, WA Mnaymneh : Clinical outcome in patients presenting with fungating soft tissue sarcomas. American Academy of Orthopaedic Surgeons 70th Annual Meeting, New Orleans LA, 2003 February.	Presentation
Temple, HT, DA Gajewski, A Mollabashy, DK Rader, WA Mnaymneh : The effects of chemotherapy on patients with high grade soft tissue sarcomas. 44th Annual Meeting of the Society of Military Orthopaedic Surgeons, San Diego CA, 2003 February.	Presentation
Tis, JE, WR Klemme, KL Kirk, KP Murphy, B Cunningham : Braided hamstring tendons for reconstruction of the anterior cruciate ligament - A biomechanical analysis. Am J Sports Med, 30(5):684-688, 2002 September-October.	Publication

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CITATION	TYPE
Wallace, RE, K Jones, B Raiffee, N Inoue, K McHale, EY Chao : Distraction osteogenesis - A densitometric, biomechanical, and histological study. Eastern Orthopaedic Association 33rd Annual Meeting, 2002 October.	Presentation
Wallace, RE, K Jones, B Raiffee, N Inoue, K McHale, EY Chao : Distraction osteogenesis - A densitometric, biomechanical, and histological study. Maryland Orthopaedic Association Annual Meeting, 2003 April.	Presentation
Wilson, LA : Instrumentation of the cervical thoracic junction (CTJ) - A biomechanical comparison of thoracic pedicle screws (TPS) versus thoracic hooks (TH) as distal anchors for long constructs. Cervical Spine Research Society 30th Annual Meeting, Miami Beach FL, 2002 December.	Presentation
<b><u>Physical Medicine and Rehabilitation Service</u></b>	
Boden, BP, W Lin, M Young, FO Mueller : Catastrophic injuries in wrestlers. Am J Sports Med, 30:791-795, 2002 November-December.	Publication
Gupta, R, J Gambel, B Schiefer : Personal protection measures against arthropods. Military Preventive Medicine - Mobilization and Deployment, Volume I (Kelley, PW ed.), Textbooks of Military Medicine, Washington DC, chapter 22, 2003.	Publication
Pasquina, PF, S Kelly : Assessing clinical competence in physical medicine and rehabilitation residency programs. Am J Phys Med Rehabil, 82:473-478, 2003.	Publication
Wallach, R, A McCarthy, P Pasquina : Esophageal migration of a percutaneous esophageal jejunostomy tube in a brain injured patient - A case report. Arch Phys Med Rehabil, 83(11):1649, 2002 November-December.	Abstract
Wallach, R, A McCarthy, P Pasquina : Esophageal migration of a percutaneous esophageal jejunostomy tube in a brain injured patient - A case report (poster). Annual 63rd AAPMR Meeting, Orlando FL, 2002 November.	Presentation
<b><u>Physical Therapy Service</u></b>	
Springer, BA, JB Bartholomew : Heart rate variability and mood following moderate intensity exercise. American College of Sports Medicine 50th Annual Meeting, San Francisco CA, 2003 May.	Presentation
Springer, BA, JB Bartholomew, A Loukas : Heart rate variability and mood following moderate intensity exercise. Medicine and Science in Sports and Exercise, 35(5):Supplement, 2003.	Abstract
<b><u>DEPARTMENT OF PATHOLOGY AND AREA LABORATORIES</u></b>	
Auerbach, M, A Auerbach, K Kaplan : A 56 year old female with a mass in the ankle - Inflammatory myxohyaline tumor of distal extremities. California Tumor Tissue Registry, Website Case of the Month, 2002 December.	Presentation
Auerbach, M, R Willard : A 22 year-old male with a solitary red calf papule - Targetoid hemosiderotic hemangioma (poster). American Academy of Dermatology Meeting, San Francisco CA, 2003.	Presentation
Auerbach, MJD, RJ Willard : Pathologic quiz case - A 23-year-old man with a solitary red calf lesion. Arch Pathol Lab Med, 127(6):e265-e266, 2003 June.	Presentation
Bassiwa, L, D Craft : Direct detection of altered penicillin binding protein (PBP2') in Staphylococcus aureus and coagulase negative staphylococci in blood culture bottles (poster). Abstr Annu Meet Am Soc Microbiol, C-86, 2003 May.	Abstract

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CITATION	TYPE
Bassiwa, L, D Craft : Direct detection of altered penicillin binding protein (PBP2') in Staphylococcus aureus and coagulase negative staphylococci in blood culture bottles (poster). 103rd General Meeting, American Society for Microbiology, 2003 May.	Presentation
Bell, C, A Eberly, A Whelen, J Perez, B Hill, W Nauschuetz, A Ewell, K Sconce, C Giron, M Martinez, K Kaplan, D Craft, H Chong, S Mahlen, D Turgeon, M Koenig, D Heath, E Ager : Multi-center evaluation of HPV reproducibility to develop consensus recommendations for repeating and reporting results (poster). 27th Annual Society of Armed Forces Medical Laboratory Scientists, Reno NV, 2003 March.	Presentation
Boardman, J, KJ Kaplan, C Hollcraft, LT Bui-Mansfield : Torsion of the epiploic appendage. Radiologic-pathologic Conference of Keller Army Community Hospital at West Point, U.S. Military Academy, 2003.	Presentation
Boardman, J, KJ Kaplan, C Hollcraft, LT Bui-Mansfield : Torsion of the epiploic appendage. AJR Am J Roentgenol, 180(3):748, 2003.	Publication
Boast, DL, KJ Kaplan, MR Henry : Effects of pregnancy on cervical dysplasia - Risks of progression and management implications. Am J Clin Pathol, 118(4):637, 2002 (FY03).	Abstract
Boast, DL, KJ Kaplan, MR Henry : Effects of pregnancy on cervical dysplasia - Risks of progression versus regression and implications for management. ASCP/CAP National Meeting, Washington DC, 2002 (FY03).	Presentation
Bui-Mansfield, LT, KJ Kaplan : Spindle cell lipoma of the upper back. Radiologic-pathologic conference of Keller Army Community Hospital at West Point, U.S. Military Academy, 2002 November.	Presentation
Bui-Mansfield, LT, KJ Kaplan : Spindle cell lipoma of the upper back. AJR Am J Roentgenol, 179(5):1158, 2002 November.	Publication
Bui-Mansfield, LT, KJ Kaplan, C Hollcraft : Calcified lymphangioma of the gonadal vein. Radiologic-pathologic conference of Keller Army Community Hospital at West Point, U.S. Military Academy, 2002 December.	Presentation
Bui-Mansfield, LT, KJ Kaplan, C Hollcraft : Calcified lymphangioma of the gonadal vein. AJR Am J Roentgenol, 179(6):1480, 2002 December.	Publication
Bui-Mansfield, LT, KJ Kaplan, J Boardman : Synovial sarcoma of the chest wall. Radiologic-pathologic conference of Keller Army Community Hospital at West Point, U.S. Military Academy, 2002 October.	Presentation
Bui-Mansfield, LT, KJ Kaplan, J Boardman : Synovial sarcoma of the chest wall. AJR Am J Roentgenol, 179(4):880, 2002 October.	Publication
Craft, D : Basic Clinical Microbiology - Workshop. 27th Annual Society of Armed Forces Medical Laboratory Scientists, Reno NV, 2003 March.	Presentation
Craft, D, J Murray, R Slater : Deployment microbiology - Workshop. 27th Annual Society of Armed Forces Medical Laboratory Scientists, Reno NV, 2003 March.	Presentation
Duncan, MB, KJ Kaplan, MT Smith : An unusual case of colonic lymphoma presenting as a diminutive colon polyp (poster). 2002 American College of Gastroenterology Annual Meeting and Postgraduate Course, Seattle WA, 2002 (FY03).	Presentation
Kaplan, K, K Sconce, D Craft : Reflex HPV testing in a military medical population. United States and Canadian Academy of Pathology Annual Meeting, 2003 March.	Presentation
Kaplan, KJ : Implementation of a worldwide telepathology service. 2002 Advancing Pathology Informatics, Imaging, and the Internet, 7th Annual Conference, Pittsburgh PA, 2002 October.	Presentation
Kaplan, KJ : Practical telepathology - Applications and implementation issues. 2002 Breakout Session, Seventh Annual Conference for Advancing Pathology Informatics, Imaging, and the Internet, Pittsburgh PA, 2002 (FY03).	Presentation

## FY 2003 PUBLICATIONS BY DEPARTMENT/SERVICE AND AUTHOR

CITATION	TYPE
Kaplan, KJ, AA Corsini : Hodgkin's-like transformation in chronic lymphocytic leukemia presenting as a liver mass diagnosed by fine-needle aspiration biopsy. South Med J, 95(12):S33-34, 2002 December.	Abstract
Kaplan, KJ, AA Corsini : Hodgkin's-like transformation in chronic lymphocytic leukemia presenting as a liver mass diagnosed by fine-needle aspiration biopsy (poster). 2002 Southern Medical Association 96th Annual Scientific Assembly, Washington DC, 2002 (FY03).	Presentation
Kaplan, KJ, AY Bolger, DL Boast : Use of robotic telepathology for liquid based cytology. Mod Path, 16(1):313, 2003.	Abstract
Kaplan, KJ, AY Bolger, DL Boast : Use of robotic telepathology for liquid based cytology (poster). 2003 USCAP/IAP National Meeting, Washington DC, 2003.	Presentation
Kaplan, KJ, BL Nelson : Myoclonic epilepsy and cognitive decline in a 19-year old man. Arch Pathol Lab Med, 127(4):e231-232, 2003.	Publication
Kaplan, KJ, DL Boast, AY Bolger : Are current image resolutions sufficient for telecytology?. Telemed J E Health, 9(S1):108, 2003.	Abstract
Kaplan, KJ, DL Boast, AY Bolger : Use of telepathology for liquid-based cytology. Arch Pathol Lab Med, 127(7):795-796, 2003.	Abstract
Kaplan, KJ, DL Boast, AY Bolger : Are current image resolutions sufficient for telecytology? (poster). 2003 American Telemedicine Association Eighth Annual Meeting & Exposition, Orlando FL, 2003.	Presentation
Kaplan, KJ, DL Boast, AY Bolger : Dynamic telepathology for use in gynecologic cytology (poster). American Society of Cytopathology 51st Annual Scientific Meeting, Orlando FL, 2003.	Presentation
Kaplan, KJ, JB Benedict, GD Sandberg, CP Myers, TR Bigott, RB Greenspan : Validation of a web-based robotic telepathology system for frozen section diagnosis. Am J Clin Path, 118(4):637-638, 2002 October.	Abstract
Kaplan, KJ, JB Benedict, GD Sandberg, CP Myers, TR Bigott, RB Greenspan : Use of robotic telepathology for frozen section diagnosis (poster). 2002 Southern Medical Association 96th Annual Scientific Assembly, Washington DC, 2002 November.	Presentation
Kaplan, KJ, JB Benedict, GD Sandberg, CP Myers, TR Bigott, RB Greenspan : Validation of a web-based robotic telepathology system for frozen section diagnosis (poster). 2002 American Society of Clinical Pathologists/College of American Pathologists, ASCP/CAP National Meeting, Washington DC, 2002 (FY03).	Presentation
Kaplan, KJ, JB Benedict, GD Sandberg, CP Myers, TR Bigott, RB Greenspan : Validation of a web-based robotic telepathology system for frozen section diagnosis (poster). 2002 American Society of Clinical Pathologists/College of American Pathologists ASCP/CAP National Meeting, Washington DC, 2002 (FY03).	Presentation
Kaplan, KJ, JR Burgess, GD Sandberg, CP Myers, TR Bigott, RB Greenspan : Use of robotic telepathology for frozen-section diagnosis - A retrospective trial of a telepathology system for intraoperative consultation. Mod Pathol, 15(11):1197-1204, 2002 November.	Publication
Kaplan, KJ, KJ Sconce, DW Craft : Reflex HPV testing in a military medical population. Mod Path, 16(1):313-314, 2003.	Abstract
Kaplan, KJ, KJ Sconce, DW Craft : Reflex HPV testing in a military medical population (poster). 2003 USCAP/IAP National Meeting, Washington DC, 2003.	Presentation
Kaplan, KJ, TR Bigott : Implementation of a world-wide real-time telepathology service. Telemed J E Health, 9(S1):107-108, 2003.	Abstract

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CITATION	TYPE
Kaplan, KJ, TR Bigott : Implementation of a world-wide real-time telepathology service. Arch Pathol Lab Med, 127(7):802-803, 2003.	Abstract
Kaplan, KJ, TR Bigott : Implementation of a world-wide real-time telepathology service. 2002 Scientific Session, Seventh Annual Conference for Advancing Pathology Informatics, Imaging, and the Internet, Pittsburgh PA, 2002 (FY03).	Presentation
Kaplan, KJ, TR Bigott : Implementation of a world-wide real-time telepathology service (poster). 2003 American Telemedicine Association Eighth Annual Meeting & Exposition, Orlando FL, 2003.	Presentation
Kaplan, KJ, TR Bigott, R Herring, DR Butler, B Williams : Expert opinions just a mouse click away - The Army Telepathology Program. 2003 Scientific Session, Eighth Annual Conference for Advancing Practice, Instruction and the Innovation Through Informatics, Pittsburgh PA, 2003.	Presentation
Verma, PS, CM Gallagher : Dyspnea on exertion, fatigue, and pallor in a 50-year old active duty soldier. Mil Med, 168:587-590, 2003.	Publication
Wells, D, KJ Kaplan : Active ossifying fibroma of the jaw. Arch Pathol Lab Med, 127(8):e359-e360, 2003.	Publication
Willard, RJ, MJD Auerbach : Targetoid hemosiderotic hemangioma (Hobnail Hemangioma). American Academy of Dermatology, San Francisco CA, 2003 May.	Presentation

### **DEPARTMENT OF PEDIATRICS**

AuYeung, K, KB Madden, A Smith, JF Urban Jr., O Levander, A Zhao, T Shea-Donohue : Selenium and vitamin E deficiencies alter intestinal epithelial cell function in mice infected with Heligmosomoides polygyrus. 37th Annual Uniformed Services Pediatric Seminar, American Academy of Pediatrics, Washington DC, 2003 March.	Presentation
Bauer, AJ, A Patel, R Terrell, K Doniparthi, M Saji, M Ringel, RM Tuttle, GL Francis : Systemic Administration of Vascular Endothelial Growth Factor (VEGF) Monoclonal Antibody Reduces Growth of Papillary Thyroid Cancer in a Nude Mouse Model. Annals of Clinical and Laboratory Science, 33:192-199, 2003.	Publication
Bauer, AJ, I Bourdeau, JA Carney, CA Stratakis : A study of apoptosis and proliferation indices in primary pigmented nodular adrenocortical disease (PPNAD) (poster). 85th Annual Meeting, The Endocrine Society, Philadelphia PA, 2003 June.	Presentation
Bauer, AJ, M Poth : Controversies in Pediatric Endocrinology. 37th Annual Uniformed Services Pediatric Seminar, American Academy of Pediatrics, Washington DC, 2003 March.	Presentation
Bauer, AJ, R Terrell, NK Doniparthi, A Patel, RM Tuttle, M Saji, MD Ringel, GL Francis : Vascular endothelial growth factor monoclonal antibody inhibits growth of anaplastic thyroid cancer xenografts in nude mice. Thyroid, 12(11):953-961, 2002 November.	Publication
Bauer, AJ, S Stergiopoulos, F Sadrini, K Griffin, Sarlis, Stratakis : Characterization of protein kinase A (PKA) and PKA type 1 . regulatory subunit gene in human thyroid tumor cell lines (poster 823). Pediatr Res, Seattle WA, 2003 May.	Presentation
Bauer, AJ, T Plum, A Helms, A Patel, RM Tuttle, GL Francis : An in vitro study to determine if the novel tumor-activated fluoropyrimidine carbamate (Capecitabine) could be used to treat thyroid carcinomas (poster). 85th Annual Meeting, The Endocrine Society, Philadelphia PA, 2003 June.	Presentation
Burklow, TR, C Yu : Industrial Chemicals: Terrorist 'Weapons of Opportunity'. Pediatr Annals, 23:231-234, 2003.	Publication

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Burklow, TR, DP Shmorhun, JA Becker : Brilliant Diagnosis: Cardiology Without the Echo. 37th Annual Uniformed Services Pediatric Seminar, American Academy of Pediatrics, Washington DC, 2003 March.	Presentation
Camp, K, G Francis, L Shropshire : Initiating a phenylalanine-controlled diet in a 5-year-old child newly diagnosed with phenylketonuria (PKU): management dilemmas and developmental outcomes. Topics in Clinical Nutrition, 18:110-115, 2003.	Publication
Camp, K, L Shropshire, G Francis : Consider inborn errors of metabolism in the differential diagnosis of children with an unusual symptom complex (poster). Uniformed Services University of the Health Sciences Graduate Student Colloquium and Faculty Senate Research Day, 2003 May.	Presentation
Cashman, JR, K Camp, PV Fennessey, et al : Biochemical and clinical aspects of the human flavin-containing monooxygenase form 3 (FMO3) related to trimethylaminuria. Current Drug Metabolism, 4:151-170, 2003.	Publication
Collura-Burke, CJ, B Speller-Brown, LJ Smith, MR Nelson, HJ Schmidt : Asthma Education and its Effect on Quality of Life (poster). J Allergy & Clin Immunol, 111:S176, 2003.	Abstract
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Creamer, KM : Building The Safety Net: Pediatric Sedation 2003. European Regional Medical Command's Fall Medical-Surgical Conference, Pediatric Track, Weinheim Germany, 2003 September.	Presentation
Creamer, KM : Should Families Witness Resuscitation? Clinical Controversies session with Col Kenneth Torrington. ACCP's 68th Annual International Scientific Assembly - Chest 2002 - San Diego CA, 2002 November.	Presentation
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Creamer, KM : Family Witnessed Resuscitation. Chest, 124(2):769-770, 2003 August.	Publication
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deLorimier, AJ, W Byrd, ER Hall, ZJ Roberts, CE McQueen, D Tang, W Vaghan, F Cassels : Murine antibody response to intranasally administered enterotoxigenic Escherichia coli colonization factor CS6. Vaccine, 21(19-20):2548-2555, 2003 June.	Publication
DiFazio, M, B Jabbari : A focused review of treatment with botulinum toxins for low back pain. Southeast Pain Care, Charlotte NC, 2003 January.	Presentation
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Eccles, T, A Patel, RM Tuttle, G Francis : Erythropoietin and erythropoietin receptor are expressed by childhood thyroid cancers. American Academy of Pediatrics, Uniformed Services Section, Washington DC, 2003 March.	Abstract
Eccles, T, R Terrell, A Patel, A Verma, RM Tuttle, G Francis : Erythropoietin and erythropoietin receptor are expressed by papillary thyroid carcinomas of children and adolescents. American Academy of Pediatrics, Uniformed Services Section, Washington DC, 2003 March.	Presentation

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Gramling, JD, KJ AuYeung, KM Camp, PL Rogers, C Maydonovitch, CA Sullivan : Obesity in Children with GERD: A Retrospective Chart Review. <i>J Pediatr Gastroenterol Nutr</i> , 37(3):337, 2003.	Abstract
Griffin, KJ, LS Kirschner, SG Stergiopoulos, SM Lenherr, ES Clafin, L Matyakhina, AJ Bauer, JA Carney, CA Stratakis : A Transgenic mouse model expressing an antisense construct to PRKAR1A: A model for Carney Complex. 85th Annual Meeting, The Endocrine Society, Philadelphia PA, 2003 June.	Presentation
Gydee, H, JT O'Neill, A Patel, A Bauer, RM Tuttle, G Francis : Differentiated thyroid carcinomas from children and adolescents express IGF-1 and IGF-1-R - Cancers with the most intense expression of IGF-1-R are more aggressive. <i>American Academy of Pediatrics, Uniformed Services Section, Washington DC</i> , 2003 March.	Abstract
Gydee, H, JT O'Neill, A Patel, RM Tuttle, G Francis : Insulin-like growth factor-1 (IGF-1) and the IGF-1 Receptor (IGF-1R) are expressed by childhood thyroid cancers and IGF-1R expression is increased in aggressive tumors. <i>American Academy of Pediatrics, Uniformed Services Section, Washington DC</i> , 2003 March.	Presentation
Katz, DE, AJ deLorimier, MK Wolf, ER Hall, FJ Cassels, JE vanHamont, RL Newcomer, MA Davachi, DN Taylor, McQueen : Oral immunization of adult volunteers with microencapsulated enterotoxigenic <i>Escherichia coli</i> (ETEC) CS6 antigen. <i>Vaccine</i> , 21:341-346, 2003 January.	Publication
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Marks, R, A Patel, J Modi, RM Tuttle, G Francis : Are proliferating thyroid cancer associated lymphocytes CD8 + killer cells?. <i>American Academy of Pediatrics, Uniformed Services Section, Washington DC</i> , 2003 March.	Presentation
Modi, J, A Patel, R Terrell, RM Tuttle, G Francis : Thyroid cancers from children and adolescents that contain a mixture of lymphocytes have a favorable prognosis. <i>American Academy of Pediatrics, Uniformed Services Section, Washington DC</i> , 2003 March.	Abstract
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Pluim, T, A Helms, A Patel, A Bauer, RM Tuttle, G Francis : An in vitro study to determine if the novel tumor activated fluoropyrimidine carbamate (Capecitabine) could be used to treat thyroid carcinomas. American Academy of Pediatrics, Uniformed Services Section, Washington DC, 2003 March.	Presentation
Powers, PA, CA Dinauer, RM Tuttle, DK Robie, DR McClellan, GL Francis : Treatment of recurrent papillary thyroid carcinoma in children and adolescents. <i>J Pediatr Endocrinol Metab</i> , 16:1033-1040, 2003.	Publication
Powers, PA, CA Dinauer, RM Tuttle, GL Francis : The MACIS score predicts the clinical course of papillary thyroid carcinoma in children and adolescents. 37th Annual Uniformed Services Pediatric Seminar, American Academy of Pediatrics, Washington DC, 2003 March.	Presentation
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Rotenberg, J, B Jabbari, M DiFazio : Movement Disord Successful Treatment of Recalcitrant Restless Leg Syndrome with Botulinum. 7th International Congress of Parkinson's Disease and Movement Disorders, 2002 November.	Presentation
Rotenberg, J, TR Burklow, JS Selanikio : Weapons Of Mass Destruction: The Decontamination Of Children. <i>Pediatr Annals</i> , 23:261-267, 2003.	Publication
Schmidt, HJ : Asthma Cases: Spacers, Nebulizers, and More. 37th Annual Uniformed Services Pediatric Seminar, American Academy of Pediatrics, Washington DC, 2003 March.	Presentation
Sutton, J : Increased risk for aplastic anemia and myelodysplastic syndrome in individuals lacking GSTT1 gene. 2003 Pediatric Academic Societies Annual Meeting, Seattle WA, 2003 May.	Presentation
Whiteman, S, T Tillman, K AuYeung, K Madden, A Chap, J Elfrey, A Zhao, T Shea-Donohue : Enteral L-Arginine attenuates the effects of diabetic hyperglycemia on colonic epithelial cell function in rats. <i>Gastroenterology</i> , 124:A261, 2003.	Abstract
Yacovone, MA, PA Powers, RK Katial : Primary autoimmune neutropenia associated with endocrinopathy. 60th Annual Meeting of the American Academy of Allergy, Asthma and Immunology, Denver CO, 2003 March.	Presentation
Yu, C, TR Burklow : Vesicants and Children. <i>Pediatr Annals</i> , 23:254-257, 2003.	Publication
<b><u>Pediatric Cardiology Service</u></b>	
Adelman, WP : Clinical practice guideline implementation - Clinical issues and special populations. Department of Defense Tobacco Use Cessation Clinical Practice Guideline, Korea Implementation Conference, Seoul, South Korea, 2002 November.	Presentation
Au Yeung, K, KB Madden, A Smith, FJ Urban Jr., O Levander, A Zhao, T Shea-Donohue : Selenium and vitamin e deficiencies alter intestinal epithelial cell function in mice infected with heligmosomoides polygyrus. 2002 Annual Meeting of the North American Society of Pediatric Gastroenterology, Hepatology, & Nutrition, San Antonio TX, 2002 October.	Presentation



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Rick, JR, C Semino-Mora, E Rueda-Pedraza, CA Sullivan, A Dubois : Relation between CagA expression and persistent helicobacter pylori infection among children and adolescents (poster). 2002 Annual Meeting of the North American Society of Pediatric Gastroenterology, Hepatology, & Nutrition, San Antonio TX, 2002 October.	Presentation
Rick, JR, MJ Cossentino, FM Moses : Familial Schatzki's ring - Case report emphasizing the etiologic considerations (poster). 2002 Annual Meeting of the North American Society of Pediatric Gastroenterology, Hepatology, & Nutrition, San Antonio TX, 2002 October.	Presentation
Robinson, A : Chlamydia update. Region 3 Infertility Project Meeting, Washington DC, 2002 October.	Presentation
Robinson, A : SAM multidisciplinary committee. Society for Adolescent Medicine Newsletter, 2002 November.	Publication
Shmorhun, DP : Arrhythmogenic right ventricular cardiomyopathy. National Capital Consortium Pediatrics Clinicopathological Conference, Washington DC, 2003 January.	Presentation
<b><u>DEPARTMENT OF PHARMACY</u></b>	
Adesuyi, OA, DA Solimando, JA Waddell : PVDA regimen for remission induction of acute lymphoblastic leukemia (ALL). Hosp Pharm, 38:544-550, 2003.	Publication
Bauer, AJ, R Terrell, A Patel, RM Tuttle, MD Ringel, GL Francis : Vascular Endothelial Growth Factor Monoclonal Antibody (VEGF-MAb) Inhibits Growth of Anaplastic Thyroid Cancer Xenografts in Nude Mice. Thyroid, 12:953-961, 2002 November.	Publication
Doulaveris, P, DA Solimando, JA Waddell : High-dose cytarabine for consolidation and relapse therapy in acute myelogenous leukemia. Hosp Pharm, 38:118-120 & 179, 2003.	Publication
Gallagher, CM, J Drabick, JA Waddell, et al : Inadvertent intravenous Bacillus Calmette-Guerin converted near-CR to CR in a patient with relapsed multiple myeloma. Blood, 102:5272, 2003.	Abstract
Iheagwara, NL, JA Waddell, DA Solimando : Cisplatin, vinblastine, and bleomycin (PVB) regimen for testicular cancer. Hosp Pharm, 38:822-827, 2003.	Publication
Moussavian, PA, DA Solimando, JA Waddell : Hoelzer regimen for therapy of adult acute lymphoblastic leukemia. Hosp Pharm, 38:436-510, 2003.	Publication
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Rutledge, MR, DA Solimando, JA Waddell : Fludarabine, cytarabine, and filgrastim (FLAG) regimen for induction therapy of acute myelogenous leukemia or myelodysplastic syndrome. Hosp Pharm, 38:320-327, 2003.	Publication
Sano, H, J Waddell, P Doulaveris, R Myhand : Standardized chemotherapy order forms. Proceedings of the Eastern States Conference for Pharmacy Residents and Preceptors, 176, 2003.	Abstract
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Solimando, DA, A Waddell : Etoposide and cisplatin (EP) for testicular cancer. Hosp Pharm, 38:921-925, 2003.	Publication
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Waddell, J, A Januszewicz, L Sutton, E Spaar, M Heath, D Solimando : Investigating adverse medication events caused by an unknown medication. J Am Pharm, 43:295-296, 2003.	Abstract
Waddell, J, A Januszewicz, L Sutton, E Spaar, M Heath, D Solimando : investigating adverse medication events caused by an unknown medication. American Pharmaceutical Association Annual Meeting, New Orleans LA, 2003 March.	Presentation
Waddell, JA, DA Solimando : Mitoxantrone, etoposide, and cytarabine (MEC) regimen for relapsed or refractory acute myelogenous leukemia. Hosp Pharm, 38:218-221, 2003.	Publication
Waddell, JA, P Doulaveris, DA Solimando : High-dose cytarabine (HIDAC) plus daunorubicin for remission induction of acute myelogenous leukemia. Hosp Pharm, 38:20-24, 2003.	Publication

### **DEPARTMENT OF PREVENTIVE MEDICINE**

Anno, G, R Bloom, JR Mercier, RW Young : Dose Response Relationships for Acute Ionizing Radiation Lethality. Health Physics, 84(5):565-575, 2003.	Publication
Hack, D : Smallpox Immunization Plan: A RMC Perspective. 7th Annual Force Health Protection Conference, Albuquerque NM, 2003 August.	Publication
Mercier, JR, SC Moss : The U.S. Army Radiological Advisory Medical Team. Proceedings of the 36th Health Physics Society Midyear Topical Meeting - Radiation Safety Aspects of Homeland Security and Emergency Response, San Antonio TX, 158-163, 2003 January.	Publication

### **DEPARTMENT OF PSYCHIATRY**

Benedek, DM : Family Violence: Risk Factors in the U.S. Military Community - Family Violence, A Military Perspective. U.S. Dept. of Justice, FBI National Center for the Analysis of Violent Crime and the Behavioral Science Unit Family Violence Symposium, Leesburg VA, 2003 August.	Presentation
Benedek, DM : Transforming Behavioral Health: Applying lessons Learned in Bosnia. Operational Mental Health Symposium, 6th Annual Force Health Protection Conference, Albuquerque NM, 2003 August.	Presentation
Benedek, DM : Medico-Legal Implications of Drug Interactions. Concise Guide to Drug Interaction Principles for Medical Practice, KL Cozza, SC Armstrong, JR Osterheld (eds), APPI Press, Washington DC, 407-418, 2003.	Publication
Benedek, DM, SC Armstrong, KL Cozza : Medico-legal Aspects of Drug-Drug Interactions - CME Course #69, Med-Psych Drug-Drug Interactions - An update. Annual Meeting of the American Psychiatric Association, San Francisco CA, 2003 May.	Presentation
Black N : Child and Adolescent Clinics of North America: The child, adolescent and family in the Hindu and Buddhist traditions. , 2003 March.	Publication
Black, N : The child soldier: the unexpected combatant. U.S. Army Behavioral Science Short Course, Albuquerque NM, 2003 August.	Presentation
Chun, RS : A Web-based Automated Mental Health Intake System for Child and Adolescent Psychiatry Service. 8th Annual Meeting and Exposition of the American Telemedicine Association, Orlando FL, 2003 April.	Presentation
Chun, RS, D Edison, A Cox, S Cozza, G Gadiyak, V Gadiyak, W Parker, S Mann, R Poropatich, D DeWitt, S Rosquist : Web-based Automated Mental Health Intake System (WAMHIS) - Examining parent and provider satisfaction. Telemedicine and e-Health J, 9(Suppl1):S-47, 2003 Spring.	Abstract

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Cozza, SJ : Developing a Clinical and Business Strategy for Telebehavioral Health. Tele Mental Health Special Interest Group Short Course, American Telemedicine Meeting, Orlando FL, 2003 April.	Presentation
Cozza, SJ : Telepsychiatry with child and adolescent patients. 46th Winter Meeting of the American Academy of Psychoanalysis and Dynamic Therapy, San Antonio TX, 2002 December.	Presentation
Cozza, SJ : Telepsychiatry with Child and Adolescent Patients. 46th Winter Meeting of the American Academy of Psychoanalysis and Dynamic Therapy, San Antonio TX, 2002 December.	Presentation
Cozza, SJ : Treatment of PTSD in children - Pharmacological and psychotherapeutic strategies. 4th Annual UC Davis Distinguished Psychiatrists Symposium, Sacramento CA, 2002 October.	Presentation
Cozza, SJ : Treatment of PTSD in Children: Pharmacological and Psychotherapeutic Strategies. 4th Annual UC Davis Distinguished Psychiatrists Symposium, Sacramento CA, 2002 October.	Presentation
Croarkin, P : From King George to Neuroglobin - The Psychiatric Aspects of Acute Intermittent Porphyria. J Psychiatric Prac, 8(6):398-405, 2002 November.	Publication
Croarkin, P : Informed Consent for Psychotherapy: A Look at Therapists' Understanding, Opinions, and Practices. Am J Psychother, 57(3):384-400, 2003 September.	Publication
Eaton, KM, CW Hoge, SC Messer, AL Garvey-Wilson, SE Lesikar : Suicide rates over the decade across civilian and military populations. American Psychiatric Association Syllabus and Proceedings from the 2003 APA Annual Meeting, 30, 2003 May.	Abstract
Garvey-Wilson, AL, CW Hoge, SC Messer, SE Lesikar, KM Eaton : Diagnoses in behavioral health clinics: impact on perceived burden of mental health. American Psychiatric Association Syllabus and Proceedings from the 2003 APA Annual Meeting, 23, 2003 May.	Abstract
Greiger, T : Community Terror: Hospital Staff Responses to a Series of Sniper Shootings. American Psychiatric Association Annual Meeting, San Francisco CA, 2003 May.	Presentation
Greiger, T : Psychiatric Consultation Following Disaster Process and Findings. Maryland Psychiatric Society Conference on Disaster, Baltimore MD, 2003 April.	Presentation
Greiger, T : Terror at Sea: Psychiatric Responses in the Crew of the USS Dolphin Following a Near Sinking. American Psychiatric Association Annual Meeting, San Francisco CA, 2003 May.	Presentation
Grieger, TA, DM Benedek, CS Fullerton, RJ Ursano : Community Terror: Hospital Staff Responses to a Series of Sniper Shootings (Poster). Annual Meeting of the American Psychiatric Association, San Francisco CA, 2003 May.	Presentation
Habben, CJ : Students, new psychologists, and licensure laws: Reasons for change and the costs of status quo - Licensure: Issues of timing, supervision, and quality of training. 111th Annual Convention of the American Psychological Association, Toronto Ontario Canada, 2003 August.	Presentation
Habben, CJ : The other side of masculinity and the future of the division. 111th Annual Convention of the American Psychological Association, Toronto Ontario Canada, 2003 August.	Presentation
Habben, CJ : Obtaining a license to practice psychology. The Portable Mentor - Expert Guide to a Successful Career in Psychology, MJ Prinstein & M Patterson (eds), Kluwer Academic/Plenum Publishers, New York NY, 181-189, 2003.	Publication
Hoge, CW : Impact of mental disorders in active duty military population - An overview of WRAIR psychiatric research program. USUHS, 2003 May.	Presentation
Hoge, CW : Introduction to Psychiatry Epidemiology. Chronic Diseases Epidemiology Course, M.P.H., USUHS, 2003 May.	Presentation

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Hoge, CW : The impact of deployment on the mental health and well-being of soldiers and their families: preliminary analysis of surveys conducted among XVIII Airborne Corps soldiers deploying to SW Asia. 6th Annual Force Health Protection Conference, Albuquerque NM, 2003 August.	Presentation
Hoge, CW, CC Engel Jr. : Research methods in psychiatry. 6th Annual Force Health Protection Conference, Albuquerque NM, 2003 August.	Presentation
Hoge, CW, SC Messer, CC Engel, M Krauss, P Amoroso, MAK Ryan, DT Orman : Priorities for psychiatric research in the U.S. military: an epidemiological approach. Mil Med, 168:182-185, 2003.	Publication
Jordan, N, C Hoge, S Tobler, J Wells, G Dydek, W Egerton : Evaluation of the Mental Health Impact of 9/11: Results from the Pentagon Post Disaster Health Assessment. Preventive Medicine Conference, San Diego CA, 2003 February.	Abstract
Labbate, L, H Croft, M Oleshansky : Antidepressant-Related Erectile Dysfunction: Management via Avoidance, Switching Antidepressants, Antidotes and Adaptation. J Clin Psychiatry, 64(suppl 10):11-19, 2003.	Publication
Lacy, TJ, DM Benedek : Weapons of Mass Destruction: Managing the Behavioral Reaction in Primary Care. South Med J, 96(4), 2003 April.	Publication
Levant, RF, CJ Habben : The new psychology of men: Application to rural men. Rural Behavioral Health Care - An Interdisciplinary Guide, B Hudnall Stamm (ed), American Psychological Association, Washington DC, 171-180, 2003.	Publication
Malone, RD, DM Benedek, RG Carr : Occupational Psychiatry Services in a Military Setting. Mil Med, 2002 December.	Publication
Messer, SC, X Liu, CW Hoge, DN Cowan, CC Engel : Projecting national survey prevalence to populations of interest. American Psychiatric Association Syllabus and Proceedings from the 2003 APA Annual Meeting, 23, 2003 May.	Abstract
Ritchie, EC, DM Benedek, RD Malone : Psychological Autopsies in the United States Military. Annual Meeting of the American Academy of Psychiatry and the Law, Newport Beach CA, 2002 October.	Presentation
Robinson, JD, CJ Habben : The role of the American Board of Professional Psychology in professional mobility. Professional Psychology - Research and Practice, 34(5):474-475, 2003.	Publication
Wain, H : An Integrative Approach to The Working Through Process in Psychotherapy Course. Annual Meeting of American Psychiatry Association, San Francisco CA, 2003 May.	Presentation
Wain, H : Hypnosis in psychiatry consultation-liaison. Society of Clinical and Experimental Hypnosis, Boston MA, 2002 November.	Presentation
Wain, H : Meeting The Patient Where They Are. Annual Meeting American Society of Clinical Hypnosis, Washington DC, 2003 March.	Presentation
Wain, H : Psychosomatic Medicine and Consultation Liaison Psychiatry. Annual Meeting Society of Clinical and Experimental Hypnosis, Boston MA, 2002 November.	Presentation
Wain, H : The Use of Hypnosis in the Diagnosis and Treatment of Atypical Dissociative Disorders. American Society of Clinical Hypnosis, Arlington VA, 2003 March.	Presentation
Wain, H : Workshop on Psychological and Medical Hypnosis. Tripler Army Medical Center, 2003 March.	Presentation
Waldrep, DA : Application of Army Combat Stress Control Doctrine in Work with Pentagon Survivors. 2003 Army Behavioral Science Short Course, Albuquerque NM, 2003 August.	Presentation

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CITATION	TYPE
Waldrep, DA : Psychological response to bioterrorism and weapons of mass destruction - Communicating the risk. Mental Health Response to WMD Terrorist Attacks Conference, Philadelphia PA, 2002 October.	Presentation
Waldrep, DA : Psychological response to bioterrorism and weapons of mass destruction - Communicating the risk. American Red Cross - Southeastern Pennsylvania Chapter, 2002 October.	Presentation
Waldrep, DA : Psychological response to bioterrorism and weapons of mass destruction - Communicating the risk. Early Responders Distance Learning Center (ERDLC), St. Joseph's University, Philadelphia PA, 2002 October.	Presentation
Waldrep, DA : Psychological response to bioterrorism and weapons of mass destruction - Communicating the risk. Philadelphia Division of the NASW PA Chapter, 2002 October.	Presentation
Waldrep, DA : Two Cases of ADHD Following GABHS Infection - A PANDA Subgroup?. J Am Academy of Child and Adolescent Psychiatry, 41:1274, 2002 November.	Publication

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Dunivin, D : Telehealth group psychosocial intervention outcomes - Breast cancer patients and partners (poster). American Telemedicine Association, Orlando FL, FY not submitted.	Presentation
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### **DEPARTMENT OF RADIOLOGY**

#### **Diagnostic Radiology Service**

Dinauer, P, D Flemming, N Gambill, T Hash, W Doukas, R Islinger, K Murphy : Detection of superior labral lesions with noncontrast high-resolution and intravenous gadolinium enhanced MRI. Society of Skeletal Radiology 26th Annual Meeting, Coronado Island CA, 2003 March.	Presentation
Dinauer, P, D Flemming, N Gambill, T Hash, W Doukas, R Islinger, K Murphy : Detection of superior labral lesions with noncontrast high-resolution and intravenous gadolinium enhanced MRI. Society of Skeletal Radiology 26th Annual Meeting, Coronado Island CA, 2003 March.	Presentation
Dinauer, P, JA Bojescul, KJ Kaplan, C Litts : Bilateral lipoma arborescence of the bicipitoradial bursa. Skeletal Radiol, 31(11):661-665, 2002 November.	Publication
Hirsch, J : Imaging of carotid artery disease - Four-year experience at one teaching hospital. International MR Angio Club XV Annual International Workshop, O'Reilly Conference Center, Dublin Ireland, 2003 September.	Presentation
Pickhardt, PJ, JH Choi : Electronic cleansing and stool tagging in CT colonography - Advantages and pitfalls with primary three-dimensional evaluation. AJR Am J Roentgenol, 181(3):799-805, 2003 September.	Publication
Rexroad, JT : The CT arrowhead sign. Radiology, 227(1):44-45, 2003 April.	Publication
Rexroad, JT, RP Moser III, J Georgia : "Fish" or "Fish-Mouth" vertebrae?. Am J Roentgenol, 181(3):886-887, 2003 September.	Publication
Riedy, G : Rapid proton fat-water spectroscopy for the characterization of non-CNS lesions in vivo. Clin Imaging, 27(3):145-149, 2003 May-June.	Publication
Riedy, G, ER Melhem : Acute infarct of the corpus callosum - Appearance on diffusion-weighted MR imaging and MR spectroscopy. J Magn Reson Imaging, 18(2):255-259, 2003 August.	Publication
Ruess, L, SC O'Connor, KH Cho, FH Hussain, WJ Howard III, RC Slaughter, A Hedge : Carpal tunnel syndrome and cubital tunnel syndrome - Work-related musculoskeletal disorders in four symptomatic radiologists. Am J Roentgenol, 181(1):37-42, 2003 July.	Publication

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CITATION	TYPE
Storm, ES : Tc99m Depreotide Imaging of Cardiac Sarcoidosis. Southern Medical Association 96th Annual Assembly, Washington DC, 2002 November.	Presentation
Storm, ES, JL Montilla, DA Kristo, RS Bridwell : Tc99m Depreotide Imaging of Cardiac Sarcoidosis. South Med J, 95(10):S38-39, 2002 October.	Abstract

### **Nuclear Medicine Service**

Soler-Montilla, JL, JT Rexroad, RS Bridwell : Tc-99m depreotide scintigraphy of low-grade non-Hodgkin's lymphoma. Clin Nucl Med, 28:503-505, 2003 June.	Publication
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### **DEPARTMENT OF SOCIAL WORK**

Bowker, J : Benefits and Compensation - Getting a Fair Share - HIV Research and Treatment - Past, Present and Future. Walter Reed Army Medical Center, Washington DC, 2002 November.	Presentation
Bowker, J : Social Work Care Management in Medical Hold. Care Manager's Conference, U.S. Army Medical Department, San Antonio TX, 2003 June.	Presentation
Bowker, J : WRAMC HIV Social Work Service. Uniform Services Social Work Conference (USSW), San Diego CA, 2003 February.	Presentation
Cabrera, D : Adverse Childhood Experiences (ACE) vs. U.S. Army. Behavioral Science Short Course, Albuquerque NM, 2003 August.	Presentation
Cepero, Y : Conducting Risk Assessment Interviews for Child Abuse. Risk Assessment Videotape, Human Development Department, Virginia Tech, Falls Church VA, 2002 December.	Presentation
Fong, D : The Traumatic Sequelae of Early Infant Separation. Uniform Services Social Work Conference (USSW), San Diego CA, 2003 February.	Presentation
Piotroski, S : Human Immunodeficiency Virus Social Work Program at the Walter Reed Army Medical Center - A Historical Perspective. Mil Med, 168(9):698-701, 2003.	Publication

### **DEPARTMENT OF SURGERY**

#### **Anesthesia-Operative Service**

Cohen, SP, TM Larkin : A giant herniated disc following intradiscal electrothermal therapy. J Spinal Disord, 15(6):537-541, 2002 December.	Publication
Cohen, SP, TM Larkin, A Salahadin, A Chang, M Stojanovic : Risk factors for failure and complications of intradiscal electrothermal therapy (IDET) - A pilot study. Spine, 28(11):1142-1147, 2003 March.	Publication

#### **Army Audiology & Speech Center**

Beck, W, D Bender, R Dunlop, G Kasewurm, B Packer, T Walden : Audiologist assistants support personnel - Task force report. American Academy of Audiology Convention Program, American Academy of Audiology, Reston VA, 2003.	Abstract
Beck, W, D Bender, R Dunlop, G Kasewurm, B Packer, T Walden : Audiologist assistants support personnel - Task force report. Annual Convention of the American Academy of Audiology, Featured Session, San Antonio TX, 2003 April.	Presentation
Boop, FA, LA Newman, JW Thompson, CK Temple : Post-operative Swallowing Function After Posterior-Fossa Craniotomy in Pediatric Patients. 2002 AANS/CNS Section on Pediatric Neurological Surgery Annual Meeting, Phoenix AZ, 2002 December.	Presentation

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CITATION	TYPE
Chandler, DW : Auditory monitoring in Department of Defense. Handbook of Standard Procedures and Best Practices for Audiology and Compensation and Pension Examinations, KC Dennis (ed.), Department of Veterans Affairs, Washington DC, 2003.	Publication
Chandler, DW, DW Grantham, MR Leek : Effects of uncertainty on auditory spatial resolution in the horizontal plane. International Workshop on Spatial and Binaural Hearing, Utrecht Netherlands, 2003 June.	Presentation
Chandler, DW, JD Casler : Operational acute acoustic trauma. Antioxidant Workshop - From Chinchillas to Marines, Naval Medical Center, San Diego CA, 2002 November.	Presentation
Cord, M, G Flamme, M Nilsson, S Soli : Significance in a clinical setting - How much is better?. American Academy of Audiology Convention Program, American Academy of Audiology, Reston VA, 2003.	Abstract
Cord, MT, G Flamme, M Nilsson, S Soli : Relationship between objective and subjective outcome measures - Significance in a clinical setting - How much is better?. Annual Convention of the American Academy of Audiology, San Antonio TX, Instructional Course, 2003 April.	Presentation
Cord, MT, RK Surr, BE Walden : Directional advantage and success in everyday life. American Academy of Audiology Convention Program, American Academy of Audiology, Reston VA, 2003.	Abstract
Cord, MT, RK Surr, BE Walden : Directional advantage and success in everyday life. Annual Convention of the American Academy of Audiology, San Antonio TX, 2003 April.	Presentation
Grant, KW : Auditory supplements to speech reading. The Acoustical Society of Japan, Speech Dynamics by Ear, Eye, Mouth and Machine - An Interdisciplinary Workshop, Kyoto Japan, 2003 June.	Presentation
Grant, KW : Auditory supplements to speech reading. IEICE Workshop, Speech Dynamics by Ear, Eye, Mouth and Machine, Advanced Telecommunications Research (ATR), Kyoto Japan, 2003 June.	Presentation
Grant, KW : Auditory supplements to speech reading. Institute for Electronics, Information, and Communication Engineers (IEICE), 2003.	Presentation
Grant, KW : Speech communication in the real world - The eyes have it!. Fall Workshop, Department of Hearing and Speech Sciences, University of Maryland, College Park MD, 2003 September.	Presentation
Grant, KW : Auditory supplements to speech reading. Institute for Electronics, Information, and Communication Engineers (IEICE), 2003.	Publication
Grant, KW : Auditory supplements to speech reading. The Acoustical Society of Japan, Speech Dynamics by Ear, Eye, Mouth and Machine - An Interdisciplinary Workshop, Kyoto Japan, 15-19, 2003 June.	Publication
Grant, KW, S Greenberg : Spectro-temporal interactions in auditory and auditory-visual speech processing. Eurospeech 2003, Geneva Switzerland, 2003 September.	Presentation
Grant, KW, S Greenberg : Spectro-temporal interactions in auditory and auditory-visual speech processing. Proceedings of Eurospeech - Time is of the Essence - Dynamic Approaches to Spoken Language, Geneva Switzerland, 1-4, 2003 September.	Publication
Grant, KW, V vanWassenhove, D Poeppel : Discrimination of auditory-visual synchrony. International Speech Communication Association (ISCA) Tutorial and Research Workshop on Audio Visual Speech Processing (AVSP), St. Jorioz France, 31-35, 2003 September.	Publication
Grant, KW, V Wassenhove, D Poeppel : Discrimination of auditory-visual synchrony. Auditory-Visual Speech Processing (AVSPP 2003), St. Jorioz France, 2003 September.	Presentation
Greenberg, S, T Arai, KW Grant : The role of the temporal dynamics in understanding spoken language. Dynamics of Speech Production and Perception, P Divenyi, K Vicsi, and G Meyer (eds.), IOS Press, 315-332, 2003.	Publication

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CITATION	TYPE
Gurevich, J : Vocal cord dysfunction syndrome. Annual American College of Chest Medicine Physicians Conference, San Diego CA, 2002 November.	Presentation
Kittel, M, O Gleich, I Hamann, M Leek, R Dooling, J Strutz : Masking by Schroeder-phase harmonic complexes in gerbils - Behavioral data. 26th Annual Midwinter Meeting, Association for Research in Otolaryngology, 219, 2003.	Abstract
Kittel, M, O Gleich, I Hamann, M Leek, R Dooling, J Strutz : Masking by Schroeder-phase harmonic complexes in gerbils - Behavioral data. Midwinter Research Meeting, Association for Research in Otolaryngology, Daytona Beach FL, 2003 February.	Presentation
Leek, M : Hearing loss and cochlear processing of complex sounds. University of British Columbia, Vancouver BC Canada, 2003 February.	Presentation
Leek, MR : Hearing loss and cochlear processing of complex sounds. Fall Workshop, Department of Hearing and Speech Sciences, University of Maryland, College Park MD, 2003 September.	Presentation
Leek, MR, RJ Dooling, O Gleich, M Dent : Discrimination of temporal fine structure by birds and mammals. International Symposium on Hearing, Dourdan France, 2003 August.	Presentation
Lentz, JJ, MR Leek : Spectral shape discrimination by hearing-impaired and normal-hearing listeners. J Acoust Soc Am, 113(3):1604-1616, 2003 March.	Publication
Logemann, JA, BR Pauloski, AW Rademaker, CL Lazarus, B Mittal, J Gaziano, L Stachowiak, E MacCrecken, LA Newman : Xerostomia - 12-month changes in saliva production and its relationship to perception and performance of swallow function, oral intake, and diet after chemoradiation. Head Neck, 25(6):432-437, 2003.	Publication
Logemann, JA, M Bacon, C Lazarus, D Lundy, LA Newman, J Sandidge, P Sullivan : Differences in dysphagia treatment based on diagnosis. American Speech-Language-Hearing Association Annual Convention, Atlanta GA, 2002 November.	Presentation
McClean, MD, SM Tasko : Association of orofacial with laryngeal and respiratory motor output during speech. Exp Brain Res, 146:481-489, 2002 October.	Publication
Mesgarani, N, KW Grant, S Shamma, R Duraiswami : Augmented intelligibility in simultaneous multi-talker environments. International Conference on Auditory Display (ICAD), Boston MA, 2003 July.	Presentation
Mesgarani, N, KW Grant, S Shamma, R Duraiswami : Augmented intelligibility in simultaneous multi-talker environments. International Conference on Auditory Display (ICAD), Boston MA, 6-9, 2003 July.	Publication
Milbrath, RL, NP Solomon : Do vocal warm-up exercises alleviate vocal fatigue?. J Speech Hear Res, 46:422-436, 2003.	Publication
Molis, MR, V Summers : Effects of high presentation levels on recognition of low- and high-frequency speech. Acoustics Research Letters Online, 4:124-128, 2003.	Publication
Mueller, HG, R Bentler, C Palmer, C Preminger, T Ricketts, R Sweetow, M Valente, BE Walden : A candid round-table discussion on modern digital hearing aids and their features. The Hearing Journal, 55:23-35, 2002 October.	Publication
Musch, H, V Summers, MR Molis : Using frequency modulation to detect dead regions - Results of a pilot experiment. Annual Meeting of the American Academy of Audiology, San Antonio TX, 2003 April.	Presentation
Newhoff, M, RK Peach, RG Schwartz, BA Stach, TC Walden : Central auditory processing disorder (CAPD) - Does it exist?. Southern California Conference on Speech, Language, and Hearing Sciences, San Diego CA, 2003 February.	Presentation



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CITATION	TYPE
Newman, L : Pediatric Dysphagia. 33rd Annual Summer Colloquium, University of the Pacific, Stockton CA, 2003 June.	Presentation
Newman, LA : Diagnosis and treatment of pediatric swallowing disorders. Armed Forces Institute of Pathology Annual ENT Course, Bethesda MD, 2003 March.	Presentation
Newman, LA : Swallowing function after organ preservation protocols for advanced head and neck cancer. Netherlands Cancer Institute, Amsterdam Netherlands, 2003 March.	Presentation
Newman, LA, MR Neuman, B Hughes, CK Temple, S Gibson, J Thompson, T Boulden, R Kaufman, F Laningham, S Lile, I Tonkin : Relationship between swallowing and cardiopulmonary function in infants. Dysphagia, 18(2):156, 2003.	Abstract
Newman, LA, MR Neuman, B Hughes, CK Temple, S Gibson, JW Thompson, T Boulden, R Kaufman, F Laningham, S Lile, I Tonkin : The relationship between swallowing and cardiopulmonary function in infants. 11th Annual Dysphagia Research Society Meeting, Miami FL, 2002 October.	Presentation
Packer, B, E Friedland, K Rahe, B Richardson, B Vento, T Walden : Supervision of audiology students - Academy task force report. American Academy of Audiology Convention Program, American Academy of Audiology, Reston VA, 2003.	Abstract
Ricketts, T, B Walden, A Dittner : Directional hearing aids - An update. American Academy of Audiology Convention Program, American Academy of Audiology, Reston VA, 2003.	Abstract
Rogers, P, C Sullivan, K Powell, K Camp : The child who won't grow - The gastrointestinal, nutritional, and feeding issues and management for the child who has feeding problems. Uniformed Services Pediatric Seminar, Washington DC, 2003 March.	Presentation
Sheppard, JJ, JC Arvedon, A Heinsen-Combs, LG McNeilly, LA Newman, MS Ziev : SLPs in the neonatal intensive care unit. American Speech-Language-Hearing Association Annual Convention, Atlanta GA, 2002 November.	Presentation
Sininger, Y, R Marsh, B Walden, L Wilber : The ethics of audiologic research and collaboration with industry. American Academy of Audiology Convention Program, American Academy of Audiology, Reston VA, 2003.	Abstract
Solomon, NP : What is vocal fatigue and what can we do about it?. Annual Convention of the Maryland Speech-Language-Hearing Association, Linthicum Heights MD, Invited Seminar, 2003 April.	Presentation
Solomon, NP, LE Glaze, RR Arnold, M vanMersbergen : Effects of a vocally fatiguing task and systemic hydration on men's voices. Journal of Voice, 17:31-46, 2003.	Publication
Summers, V : Effects of high presentation levels on recognition of low and high frequency speech. 26th Annual Midwinter Meeting, Association for Research in Otolaryngology, 214, 2003.	Abstract
Summers, V : Cochlear processing in high- and low frequency regions - Two cochleae in one?. Fall Workshop, Department of Hearing and Speech Sciences, University of Maryland, College Park MD, 2003 September.	Presentation
Summers, V, E deBoer, AL Nuttall : Basilar membrane responses to multicomponent (Schroeder-phase) signals - Understanding intensity effects. J Acoust Soc Am, 114:294-306, 2003.	Publication
Summers, V, M Molis : Effects of high presentation levels on recognition of low and high frequency speech. Midwinter Research Meeting, Association for Research in Otolaryngology, Daytona Beach FL, 2003 February.	Abstract

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CITATION	TYPE
Summers, V, M Molis : Effects of high presentation levels on recognition of low and high frequency speech. 24th Annual Midwinter Research Meeting of the Association for Research in Otolaryngology, Daytona Beach FL, 2003 February.	Presentation
Summers, V, MR Molis, H Musch, BE Walden, RK Surr, MT Cord : Psychophysical tuning curves and tone detection in threshold-equalizing noise. Ear and Hearing, 24:133-142, 2003.	Publication
Summers, V, T Baer, T Trine : Cochlear dead regions - Assessment and clinical implications. American Academy of Audiology Convention Program, American Academy of Audiology, Reston VA, 2003.	Abstract
Summers, V, T Baer, T Trine, V Summers : Cochlear dead regions - Some remaining questions - Cochlear Dead Regions - Assessment and Clinical Implications. Annual Convention of the American Academy of Audiology, San Antonio TX, Featured Session, 2003 April.	Presentation
Thach, BT, LA Newman, MA Lefton-Greif, CK Temple : Apnea of prematurity and feeding related apnea in pre-term infants. American Speech-Language-Hearing Association Annual Convention, Atlanta GA, 2002 November.	Presentation
Tufts, JB, T Frank : Speech production in noise with and without hearing protection. J Acoust Soc Am, 114:1067-1080, 2003.	Publication
vanWassenhove, V, KW Grant, D Poeppel : Electrophysiology of auditory-visual speech integration. International Speech Communication Association (ISCA) Tutorial and Research Workshop on Audio Visual Speech Processing (AVSP), St. Jorioz France, 37-42, 2003 September.	Publication
Walden, BE : Directional microphones and everyday listening. Bill Wilkerson Center, Vanderbilt University Medical Center, Nashville TN, 2003 July.	Presentation
Walden, BE : Everyday performance of directional microphone hearing aids. Fall Workshop, Department of Hearing and Speech Sciences, University of Maryland, College Park MD, 2003 September.	Presentation
Walden, BE : Professional ethics. Au.D. Colloquium, Bill Wilkerson Center, Vanderbilt University Medical Center, Nashville TN, 2003 March.	Presentation
Walden, BE : Predicting hearing aid microphone preference in everyday listening. Technical Report to GN ReSound, WRAMC AASC, Washington DC, 2002 (FY03).	Publication
Walden, BE, MT Cord, RK Surr, O Dyrland : Predicting hearing aid microphone preferences in daily life. Theme Hearing Conference, Stockholm Sweden, 2003 May.	Presentation
Walden, BE, RA Surr, MT Cord, O Dyrland, L Olson, T Ricketts, B Walden, A Dittberner : Predicting hearing aid microphone preferences in daily life - Directional hearing aids - An update. Annual Convention of the American Academy of Audiology, San Antonio TX, Featured Session, 2003 April.	Presentation
Walden, BE, RK Surr, MT Cord : Predicting hearing aid directional microphone performance in everyday listening. Southern California Conference on Speech, Language, and Hearing Sciences, San Diego CA, 2003 February.	Presentation
Walden, BE, Y Sininger, R Marsh, B Walden, L Wilber : Conflict of interest in product-oriented outcomes research - The ethics of audiologic research and collaboration with industry. Annual Convention of the American Academy of Audiology, San Antonio TX, Featured Session, 2003 April.	Presentation
Walden, TC : A clinical protocol for fitting amplification to the adult hearing-impaired patient. Bill Wilkerson Center, Vanderbilt University Medical Center, Nashville TN, 2003 July.	Presentation
Walden, TC, B Packer, E Friedland, F Rahe, K Richardson, B Vento, T Walden : Supervisor's expectations - Supervision of audiology students - academy task force report. Annual Convention of the American Academy of Audiology, San Antonio TX, Instructional Course, 2003 April.	Presentation

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CITATION	TYPE
Walden, TC, BE Walden : Predicting hearing aid microphone preferences in everyday listening. Annual Convention of the American Academy of Audiology, San Antonio TX, 2003 April.	Abstract
Walden, TC, BE Walden : Predicting hearing and usefulness. American Academy of Audiology Convention Program, American Academy of Audiology, Reston VA, 2003.	Abstract
Walden, TC, BE Walden : Predicting hearing and usefulness. Annual Convention of the American Academy of Audiology, San Antonio TX, 2003 April.	Presentation
<b><u>Cardiothoracic Surgery Service</u></b>	
Gadiyak, G, CR Mulligan Jr., RK Poropatich : Development of a web-based tele-consult thoracic tumor board system. American Thoracic Society, Orlando FL, 2003 April.	Abstract
Mulligan, CR Jr. : Intraoperative probes and depreotide in the staging and diagnosis of lung cancer. ADVANCE for Imaging and Radiation Therapy Professionals, 2003 March.	Others
Mulligan, CR Jr., RS Bridwell, J Montilla : Intraoperative staging of lung cancer using the gamma probe and TC99M depreotide - A feasibility study. Western Thoracic Surgical Society, Carlsbad CA, 2003 June.	Abstract
<b><u>Critical Care Medicine Service</u></b>	
Helman, DJ, JH Sherner, TM Fitzpatrick, AF Shorr : Effect of computerized standard orders on positioning of the head in bed in ventilated patients (poster). American College of Chest Physicians National Meeting, San Diego CA, 2002 November.	Presentation
Helman, DL, A Preen, NA Huepchen, AF Shorr : Successful management of a pregnant patient with idiopathic pulmonary hemosiderosis. American College of Chest Physicians National Meeting, San Diego CA, 2002 November.	Presentation
Helman, DL, RM Peckham, AF Shorr : Clinical criteria for a diagnosis of idiopathic pulmonary fibrosis - A study of interobserver variability. American College of Chest Physicians National Meeting, San Diego CA, 2002 November.	Presentation
Jackson, E : A novel diagnostic modality for acute pulmonary embolism. American College of Chest Physicians National Meeting, San Diego CA, Affiliates Presentation, 2002 November.	Presentation
Jackson, WL : Recruitment Maneuvers Should Be Done Routinely in Patients with Acute Lung Injury/ARDS: Lung Recruitment and the ARDSNet ALVEOLI Trial (Pro). Chest 2002 Clinical Controversy Pro-Con Session, American College of Chest Physicians, San Diego CA, 2002 November.	Presentation
Jackson, WL Jr. : Prospective studies are required prior to revision of perioperative transfusion guidelines. Arch Intern Med, 163:2396, 2003.	Publication
Johnson, S : Pro-Con discussion - Open lung biopsy is necessary in all patients with clinical IPF before therapy with cytotoxic agents is initiated. Army ACP National Meeting, Washington DC, 2002 November.	Presentation
Nicholson, KM, DL Helman, SD Barnett, BM Moran, SD Nathan : Effect of interferon gamma on rates of change of lung function in idiopathic pulmonary fibrosis. American College of Chest Physicians National Meeting, San Diego CA, 2002 November.	Presentation
Peckham, RM, DL Helman, AF Shorr : Potential limitations of clinical criteria for the diagnosis of idiopathic pulmonary fibrosis. American College of Chest Physicians National Meeting, San Diego CA, 2002 November.	Presentation
Popa, C : Anaphylaxis. University of Nebraska Medical Center, Family Practice Grand Rounds, Omaha NE, 2003 September.	Presentation

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CITATION	TYPE
Popa, C : Anesthetic considerations for chemical agent casualties. American Society of Anesthesiologists, Orlando FL, 2002 October.	Presentation
Popa, C : Care of the Chemical Casualty. Annual Army Anesthesiology Update, San Antonio TX, 2003 February.	Presentation
Popa, C : Workshop on Conscious Sedation. Omaha VA Medical Center, Omaha NE, 2003 September.	Presentation
Shorr, AF, AS Ramage, WL Jackson, MH Kollef : Levofloxacin for ventilator-associated pneumonia. Chest, 124:80S, 2003.	Abstract
<b><u>General Surgery Service</u></b>	
Antonellis, A, RE Ellsworth, N Sambughin, I Puls, A Abel, SQ Lee-Lin, A Jordanova, L Kremesky, K Christodoulou, LT Middleton, K Sivakuma, V Ionasescu, B Funalot, JM Vance, LG Goldfarb, KH Fishbeck, ED Green : Glycyl tRNA synthetase mutations in Charcot-Marie-Tooth disease type 2D and distal spinal muscular atrophy type V. Am J of Hum Genet, 72(5):1293-1299, 2003.	Publication
Arciero, C, C Shriver, J Somiari, R Hooke, R Somiari : Classification of breast disease by quantitative RT-PCR analysis of multiple transcripts in blood (poster). 3rd Annual CBCP Offsite, 2002 December.	Presentation
Arciero, C, C Shriver, S Somiari, J Hooke, R Somiari : Classification of breast disease by quantitative RT-PCR analysis of multiple transcripts in blood. 25th Annual Meeting, San Antonio Breast Cancer Symposium, San Antonio TX, 2002 December.	Presentation
Arciero, C, C Shriver, S Somiari, J Hooke, R Somiari : Classification of breast disease by quantitative RT-PCR analysis of multiple transcripts in blood (poster). 25th Annual Meeting, San Antonio Breast Cancer Symposium, San Antonio TX, 2002 December.	Presentation
Arciero, CA, C Shriver, G Garguilo, C Heckman, C Hooke, RI Somiari : Matrix metalloproteinase 2 and 9 activity in blood of patients with breast disease and at risk for development of breast disease (poster). Keystone Immunology Symposium, Keystone CO, 2003 February.	Presentation
Beyer, AR, RE Ellsworth, SM Lubert, J He, B Deyarmin, DL Ellsworth : Screening for TP53 gene mutations in non-neoplastic and tumorigenic breast tissue. Pittsburgh Tissue Engineering Initiative, 2003 Summer Internship Program, Pittsburgh PA, 2003 August.	Presentation
Brzeski, H, R Katenhusen, AG Sullivan, A George, RI Somiari, C Shriver : A Novel Albumin Removal Method for Improved Plasma Protein Expression Analysis in the Treatment of Amyotrophic Lateral Sclerosis Using 2D-DIGE-MS. Proceedings of the 51st American Society for Mass Spectrometry Annual Meeting, Montreal Canada, 2003.	Presentation
Brzeski, H, RA Katenhusen, AG Sullivan, A George, RI Somiari, C Shriver : A Novel Albumin Removal Method for Improved Plasma Protein Expression Analysis in the Treatment of Amyotrophic Lateral Sclerosis Using 2D-DIGE-MS (Poster). 51st Annual Conference on Mass Spectrometry and Allied Topics, Montreal Canada, 2003 June.	Presentation
Buchowiecka, A : Glycoprotein detection in breast disease (poster). 3rd Annual CBCP Offsite, 2002 December.	Presentation
Deng, B, QH Ru, GA Luo : Monitoring the unfolding and refolding of creatine kinase by capillary zone electrophoresis. J Capillary Electrophor, 8(1-2):7-10, 2003 January-April.	Publication
Ellsworth, D : Loss of heterozygosity in normal tissue adjacent to primary breast carcinoma (poster). 3rd Annual CBCP Offsite, 2002 December.	Presentation

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CITATION	TYPE
Ellsworth, DL : Impact of the human genome project on epidemiologic research. Human Genome Epidemiology Workshop: Developing Guidelines for Evaluating and Integrating Data on Using Genetic Information to Improve Health and Prevent Disease. Centers for Disease Control and Prevention, Atlanta GA, 2003 May.	Presentation
Ellsworth, DL, CD Shriver, RE Ellsworth, B Deyarmin, RI Somiari : Laser Capture Microdissection of Paraffin-Embedded Tissues. Biotechniques, 34(1):42-44, 46, 2003 January.	Publication
Ellsworth, DL, CJ O'Donnell : Emerging genomic technologies and analytic methods for population- and clinic-based research - (Human genome epidemiology). Human Genome Epidemiology - A scientific foundation for using genetic information to improve health and prevent disease, Khoury MJ, Little JB, (eds), Oxford University Press, 17-37, 2003.	Publication
Ellsworth, DL, RE Ellsworth, B Deyarmin, V Mittal, S Lubert, C Shriver, RI Somiari : Loss of heterozygosity in normal tissue adjacent to primary breast carcinomas (poster). 25th Annual Meeting, San Antonio Breast Cancer Symposium, San Antonio TX, 2002 December.	Presentation
Ellsworth, DL, RE Ellsworth, B Deyarmin, V Mittal, S Lubert, CD Shriver, RI Somiari : Loss of heterozygosity in normal tissue adjacent to primary breast carcinomas. Breast Cancer Res Treat, 76:S58, 2002 November-December.	Abstract
Ellsworth, DL, RE Ellsworth, B Deyarmin, V Mittal, S Lubert, CD Shriver, RI Somiari : Genomic loss of heterozygosity analyses as a novel method of defining surgical margins in breast cancer treatment (Poster). Society of Surgical Oncology 56th Annual Cancer Symposium, Los Angeles CA, 2003 March.	Presentation
Ellsworth, DL, RE Ellsworth, B Deyarmin, V Mittal, S Lubert, J Hooke, RI Somiari, CD Shriver : Genomic loss of heterozygosity analyses as a novel method of defining surgical margins in breast cancer treatment. Ann Surg Oncol, 10:S52, 2003.	Abstract
Ellsworth, DL, RE Ellsworth, B Love, B Deyarmin, SM Lubert, V Mittal, RI Somiari, CD Shriver : Genomic patterns of loss of heterozygosity in disease free stroma adjacent to primary breast carcinomas: potential clues to cancer development and metastasis. Integrated Biomedical Informatics and Enabling Technologies Symposium, Johnstown PA, 2003 August.	Presentation
Ellsworth, R : Loss of heterozygosity in premalignant lesions and invasive tumors of the breast - Examination of 26 commonly deleted chromosomal regions. 25th Annual Meeting, San Antonio Breast Cancer Symposium, San Antonio TX, 2002 December.	Presentation
Ellsworth, R : Loss of heterozygosity in premalignant lesions and invasive tumors of the breast - Examination of 26 commonly deleted regions (poster). 3rd Annual CBCP Offsite, 2002 December.	Presentation
Ellsworth, R, C Shriver, D Ellsworth, B Deyarmin, V Mittal, S Lubert, R Somiari : High through-put genotyping of premalignant lesions and invasive tumors of the breast. 25th Annual Meeting, San Antonio Breast Cancer Symposium, San Antonio TX, 2002 December.	Presentation
Ellsworth, R, C Shriver, D Ellsworth, B Deyarmin, V Mittal, S Lubert, R Somiari : High through-put genotyping of premalignant lesions and invasive tumors of the breast (poster). 25th Annual Meeting, San Antonio Breast Cancer Symposium, San Antonio TX, 2002 December.	Presentation
Ellsworth, RE, CD Shriver, DL Ellsworth, B Deyarmin, V Mittal, S Lubert, RI Somiari : Loss of heterozygosity in pre-malignant lesions and invasive tumors of the breast - Examination of 26 commonly deleted regions. Breast Cancer Res Treat, 76:S123, 2002 November-December.	Abstract
Ellsworth, RE, CD Shriver, DL Ellsworth, B Deyarmin, V Mittal, S Lubert, RI Somiari : Loss of heterozygosity in normal tissue adjacent to primary breast carcinomas. The American Society of Human Genetics 52nd Annual Meeting, Baltimore MD, 2002 October.	Presentation

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Ellsworth, RE, CD Shriver, DL Ellsworth, B Deyarmin, V Mittal, S Lubert, RI Somiari : Loss of heterozygosity in normal tissue adjacent to primary breast carcinomas. The 25th Annual San Antonio Breast Cancer Symposium, San Antonio TX, 2002 December.	Presentation
Ellsworth, RE, CD Shriver, DL Ellsworth, B Deyarmin, V Mittal, S Lubert, RI Somiari : Loss of heterozygosity in premalignant lesions and invasive tumors of the breast - examination of 26 commonly deleted chromosomal regions. The American Society of Human Genetics 52nd Annual Meeting, Baltimore MD, 2002 October.	Presentation
Ellsworth, RE, CD Shriver, DL Ellsworth, B Deyarmin, V Mittal, S Lubert, RI Somiari : Loss of heterozygosity in premalignant lesions and invasive tumors of the breast - examination of 26 commonly deleted chromosomal regions. The 25th Annual San Antonio Breast Cancer Symposium, San Antonio TX, 2002 December.	Presentation
Ellsworth, RE, DL Ellsworth, SM Lubert, J Hooke, IR Somiari, Shriver : High-Throughput Loss of Heterozygosity Mapping in 26 Commonly Deleted Regions in Breast Cancer. Cancer Epidemiol Biomarkers Prev, 12(9):915-919, 2003 September.	Publication
Ellsworth, RE, DL Ellsworth, SM Lubert, J Hooke, R Somiari, CD Shriver : High-throughput loss of heterozygosity mapping in 26 commonly deleted regions in breast cancer. Cancer Epidemiol Biomark Prev, 2003 September.	Publication
Ellsworth, RE, DL Ellsworth, SM Lubert, J Hooke, RI Somiari, CD Shriver : High-throughput loss of heterozygosity mapping in 26 commonly deleted regions in breast cancer. Cancer Epidemiol Biomark Prev, 12:915-919, 2003.	Publication
Gurney, JM, CD Shriver, GE Peoples : In Vivo Evidence of Epitope Spreading in Breast Cancer Patients Receiving a Preventative HER2/neu Peptide Vaccine. Gary P. Wratten Military Surgical Symposium, 2003 May.	Presentation
Gurney, JM, MM Woll, CE Storrer, CM Fisher, CD Shriver, S Ponniah, GE Peoples : In vivo Expansion of Tumor-Specific CD8+ T Cells and Intra-Antigenic Epitope Spreading in Breast Cancer Patients Receiving a Preventive HER2/neu E75 Peptide Vaccine. 94th Annual Meeting of the American Association for Cancer Research - Cancer Vaccines Mini Symposium - AACR Annual Meeting, Washington DC, 2003 July	Presentation
Gurney, JM, MM Woll, CE Storrer, CM Fisher, CD Shriver, S Ponniah, GE Peoples : In vivo Peptide Specific CD8+ Clonal Expansion and Epitope Spreading in Breast Cancer Patients Receiving a HER2/neu Peptide Vaccine (Poster). USUHS Tenth Annual Research Day Poster Session, 2003 May.	Presentation
Gurney, JM, MM Woll, CM Fisher, N Penn, DG McLeod, J Moul, CD Shriver, S Ponniah, GE Peoples : In Vivo Evidence of Epitope Spreading in Breast and Prostate Cancer Patients Receiving a Preventative HER2/neu Peptide Vaccine. 54th Annual Meeting of the Society of Surgical Oncology Cancer Forum, 2003 March.	Presentation
Hai, H, S Somiari, C Heckman, R Jordan, CD Shriver, R Somiari : Development of statistical models to predict breast cancer diseases with blood MMP levels. Integrated Bio-medical Informatics and Enabling Technologies, Pasquerilla Conference Center, Johnstown PA, 2003.	Presentation
Henkin, L, RN Bergman, DW Bowden, DL Ellsworth, SM Haffner, CD Langefeld, BD Mitchell, JM Norris, M Rewers, MF Saad, E Stamm, LE Wagenknecht, SS Rich : Genetic epidemiology of insulin resistance and visceral adiposity - The IRAS Family Study design and methods. Ann Epidemiol, 13:211-217, 2003.	Publication
Hooke, J, CD Shriver : The CBCP Tissue Repository (poster). National Consortium of Breast Centers Annual Meeting, Las Vegas NV, 2003 February.	Presentation

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CITATION	TYPE
Jing, H, K Parikh, S Somiari, R Ellsworth, C Heckman, J Hooke, C Shriver, RI Somiari : Comparative Genomic Hybridization analysis of infiltrating ductal carcinoma of the breast (Poster). Integrated Bio-medical Informatics and Enabling Technologies Showcase for Biotechnology, 2003.	Presentation
Jordan, R, L Malicki, S Somiari, H Hu, H Brzeski, D Ellsworth, C Shriver, RI Somiari : Performance of variable length oligonucleotide probes in spotted DNA microarrays (Poster). Integrated Bio-medical Informatics and Enabling Technologies Showcase for Biotechnology, 2003.	Presentation
Lubert, S, L Malicki, R Jordan, S Somiari, H Hu, H Brzeski, C Shriver, RI Somiari : Construction and microarray analysis of a subtracted breast tumor cDNA library (Poster). Integrated Bio-medical Informatics and Enabling Technologies Showcase for Biotechnology, 2003.	Presentation
Marrogi, AJ, A Ghias, L Pedraza, K Sentrayan, J Hooke, H Chandra, A Ghias, C Shriver : Oxidative and Nitrosative Stress In Breast Carcinogenesis (Poster). National Consortium of Breast Centers Annual Meeting, Las Vegas NV, 2003 February.	Presentation
Peoples, G, M Woll, C Fisher, G Ryan, D McLeod, J Moul, C Shriver, S Ponniah : Immunologic monitoring of breast and prostate cancer patients receiving a preventive HER2/neu peptide vaccine. American Association for Cancer Research "Frontiers in Cancer Prevention Research", Boston MA, 2002 October.	Presentation
Phulwani, P, A Sullivan, D Rosendale, C Ru, H Brzeski, C Shriver, R Somiari, H Hu : Development of a MASCOT parser in analyzing tandem MS data in a high throughput 2D-DIGE/MS protein identification environment (Poster). Integrated Bio-medical Informatics and Enabling Technologies, Pasquerilla Conference Center, Johnstown PA, 2003.	Presentation
Ponniah, S : The Clinical Breast Care Project - Working to treat and prevent breast cancer through vaccination. Open Door Program Seminar - Y-Me Breast Cancer Foundation, 2003 May.	Presentation
Ponniah, S, C Shriver, G Peoples : Immunotherapy for breast cancer - Clinical trials and vaccine discovery and development. NCBC Annual Meeting, 2003 February.	Presentation
Ponniah, S, C Storrer, J Gahan, J Gurney, M Woll, C Fisher, J Moul, D McLeod, C Shriver, G Peoples : Evidence of in vivo epitope spreading in breast and prostate cancer patients receiving a HER2-neu single peptide vaccine. Keystone Symposia - Basic Aspects of Tumor Immunology, Keystone CO, 2003 February.	Presentation
Ponniah, S, CD Shriver, GE Peoples : Immunotherapy for Breast Cancer: Clinical Trials and Vaccine Discovery and Development. National Coalition of Breast Centers Annual Meeting, 2003 February.	Presentation
Ponniah, S, CE Storrer, JC Gahan, JM Gurney, MM Woll, CM Fisher, J Moul, DG McLeod, CD Shriver, GE Peoples : Evidence of In Vivo Epitope Spreading in Breast and Prostate Cancer Patients Receiving a HER2/neu Single Peptide Vaccine (Poster). Keystone Symposia - Basic Aspects of Tumor Immunology, Keystone CO, 2003 February.	Presentation
Post, RJ, PK Flook, AL Millest, RA Cheke, PJ McCall, MD Wilson, M Mustapha, S Somiari, JB Davies, RA Mank, P Geene, P Enyong, A Sima, J Mas : Cytotaxonomy, morphology and molecular systematics of the Bioko form of Simulium yahense (Diptera: Simuliidae). Bulletin of Entomological Research, 93:145-157, 2003.	Publication
Ru, QH, TG Sullivan, S Russell, S Somiari, R Somiari, CD Shriver : Development of 2D LC-MS/MS and Related Bio-Technologies in the Discovery of Biomarkers for Breast Cancer. Gordon Research Conference - New Frontiers in Cancer Detection & Diagnosis, Proctor NH, 2003 August.	Abstract
Sathibalan, P, CD Shriver, GE Peoples : Immunotherapy for Breast Cancer - Clinical Trials and Vaccine Discovery and Development (Poster). National Consortium of Breast Centers Annual Meeting, Las Vegas NV, 2003 February.	Presentation

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Shriver, C, A Sullivan, S Somiari, S Russell, C Heckman, J Hooke, R Somiari : Proteomic analysis of breast tumors and associated lymph nodes by 2-dimensional-difference in-gel electrophoresis. Society of Surgical Oncology Annual Meeting, 2003 March.	Presentation
Shriver, CD : Genomics and proteomics for today's breast centers. National Consortium of Breast Centers Annual Meeting, Las Vegas NV, 2003 February.	Presentation
Shriver, CD : Surfing the Net...the use of the Internet for Surgical Education. Annual American College of Surgeons Metropolitan Washington Chapter All-Surgeons Day, Bethesda MD, 2003 March.	Presentation
Shriver, CD, R Somiari, A Hapner : Translational Research in a Breast Center with high-throughput Genomics and Proteomics (poster). National Consortium of Breast Centers Annual Meeting, Las Vegas NV, 2003 February.	Presentation
Somiari, R : Defining the molecular fingerprint of breast disease (poster). 3rd Annual CBCP Offsite, 2002 December.	Presentation
Somiari, RI, A Sullivan, S Russell, S Somiari, H Hu, R Jordan, A George, R Katenhusen, A Buchowiecka, H Brzeski, J Hooke, C Shriver : High-throughput proteomics analysis of human infiltrating ductal carcinoma of the breast. Proteomics, 3:1863-1873, 2003.	Publication
Somiari, RI, A Sullivan, S Somiari, S Russell, L Malicki, C Arciero, J Hooke, C Shriver : High through-put global abnormalities associated with breast disease. San Antonio Breast Cancer Symposium, TX, 2002 December.	Presentation
Somiari, RI, A Sullivan, S Somiari, S Russell, L Malicki, C Arciero, J Hooke, D Ellsworth, C Shriver : High through-put global analysis of abnormalities associated with breast disease. 25th Annual Meeting, San Antonio Breast Cancer Symposium, San Antonio TX, 2002 December.	Presentation
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Somiari, S, C Shriver, C Heckman, R Jordan, C Arciero, J Hooke, C Olsen, G Garguilo, RI Somiari : Active and Total MMP2 and MMP9 Levels in Plasma of Patients with Breast Cancer, Benign Disease and at Risk of Developing Breast Cancer. United States Military Cancer Center Scientific Colloquium, USUHS, 2003 September.	Presentation
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Somiari, S, C Shriver, J Hooke, J Bombatch, B Deyarmin, M Kush, R Somiari : Tissue Repository for High Throughput Genomics and Proteomics Research. 2003 Annual Meeting of International Society for Biological and Environmental Repositories (ISBER), Philadelphia PA, 2003 May.	Presentation
Storrer, CE, JM Gurney, L Kotula, JC Gahan, MM Woll, CM Fisher, CD Shriver, GE Peoples, S Ponniah : Flow Cytometry Analysis of Viral and Vaccine-Specific CD8 T Cells Using the HLA-A2:Ig Dimer Assay (Poster). 90th Annual Meeting of the American Association of Immunologists, 2003 May.	Presentation
Sullivan, A : High through-put quantitative proteomics of human breast cancer tissue using 2D-differential in-gel electrophoresis and mass spectrometry (poster). 3rd Annual CBCP Offsite, 2002 December.	Presentation
Sullivan, A, S Russell, R Jordan, J Hooke, C Shriver, R Somiari : High through-put quantitative proteomics of human breast cancer tissue using 2D-differential in-gel electrophoresis and mass spectrometry. 25th Annual Meeting, San Antonio Breast Cancer Symposium, San Antonio TX, 2002 December.	Presentation
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Sullivan, AG, S Russell, R Jordan, J Hooke, C Shriver, RI Somiari : High through-put quantitative proteomics of human breast cancer tissue using 2D-differential in-gel electrophoresis and mass spectrometry (poster). 25th Annual Meeting, San Antonio Breast Cancer Symposium, San Antonio TX, 2002 December.	Presentation
Woll, MM, CM Fisher, GB Ryan, DG McLeod, J Moul, CD Shriver, S Ponniah, GE Peoples : Immunologic Monitoring of Breast and Prostate Cancer Patients Receiving a Preventive HER2/neu Peptide Vaccine. American Association for Cancer Research's Frontiers in Cancer Prevention Research, Boston MA, 2002 October.	Presentation
Yi, S, DL Ellsworth, WH Li : Slow molecular clocks in Old World monkeys, apes, and humans. Mol Biol Evol, 19:2191-2198, 2002 December.	Publication
<b><u>Neurosurgery Service</u></b>	
Antoine, CL, RR Moquin : The Need for and Design of a Standardized Neurosurgical Database and Software Program (Poster). World Spine II International Conference, Chicago IL, 2003 August.	Presentation
Choi, J, J Ecklund, G Feolo, R Moquin, R Harbick, C Clifford, L Korenman : Wireless Teleradiology in Acute Brain and Cervical Spine Injury. American Telemedicine Association, Orlando FL, 2003 April.	Abstract
Choi, JY, JM Ecklund, RR Moquin, CD Clifford, R Harbick, LM Korenman, R Poropatich : Wireless Teleradiology in Acute Brain and Cervical Spine Injury (Poster). American Telemedicine Association Annual Meeting, Orlando FL, 2003 April.	Presentation
Ecklund, J : Historical Background and Guidelines for the Management of Penetrating Head Injury. Military Neurotrauma Conference, Bethesda MD, 2003 June.	Presentation
Ecklund, J : Injury Assessment Methods. International Conference on Closed Head Trauma, San Juan Puerto Rico, 2003 January.	Presentation
Ecklund, J : Lumbar Discectomy. Emerging Technologies in Spinal Surgery Meeting, Washington DC, 2002 October.	Presentation

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Ecklund, J : Lumbar Pedicle Anatomy and Screw Placement. 15th Annual Spine and Peripheral Nerve Course, Bethesda MD, 2003 June.	Presentation
Ecklund, J : Military Neurosurgery. John Hopkins University, Baltimore MD, 2002 October.	Presentation
Ecklund, J : Military Neurosurgery and the Defense and Veterans Brain Injury Center. Traumatic Brain Injury Symposium, Capital Hill, Washington DC, 2002 October.	Presentation
Ecklund, J : Pathophysiology of Penetrating Brain Injury. International Conference on Closed Head Trauma, San Juan Puerto Rico, 2003 January.	Presentation
Ecklund, J : Uniformed Services University Division of Neurological Surgery. 25th Anniversary and International Surgery Symposium, USUHS, Bethesda MD, 2002 October.	Presentation
Frank, E, J Martin, F Hsu : An endoscopic curved Kerrison rongeur for spinal stenosis surgery. Minim Invas Neurosurg, 45:254-256, 2002 (FY03).	Publication
Ling, G, R Riechers, M Krishna, J Blanchard, M Rosner, R Riechers Jr., C Yun, P Garcia-Pinto, K Day, K Song, A Jarell, P Rhee, J Ecklund, T Fitzpatrick, S Lockhart : Diagnosis of compartment syndrome using a microwave based detector. Proc Int'l Optical Engineering, 4744:118-124, 2002 (FY03).	Publication
Martin, JE, J Gilhooly, RR Moquin : Correction of Short-Segment Thoracic Kyphosis Utilizing Corpectomy Via Lateral Extracavitary Approach (Poster). Joint Section for Spinal and Peripheral Nerve of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons, Tampa FL, 2003 March.	Presentation
Martin, JE, J Gilhooly, RR Moquin : Surgical Correction of Short-Segment Thoracic Kyphosis with Thoracic Corpectomy Via Lateral Extracavitary Approach. Southern Neurosurgical Society Annual Meeting, Orlando FL, 2003 March.	Presentation
Martin, JE, J Gilhooly, RR Moquin : Surgical Correction of Short-Segment Thoracic Kyphosis with Thoracic Corpectomy Via Lateral Extracavitary Approach. International Meeting on Advanced Spine Techniques, Rome Italy, 2003 July.	Presentation
Martin, JE, JE Gilhooly, RR Moquin : Surgical correction of short-segment kyphosis with thoracic corpectomy via lateral extracavitary approach (poster). AANS/CNS Section on Disorders of Spine and Peripheral Nerve Annual Meeting, Orlando FL, 2003 March.	Presentation
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Martin, JE, JE Monacci : Metastatic disease of the cranial cervical junction. Textbook of Neurological Surgery - Principles and Practice, HH Batjer, CM Loftus (eds), Lippincott, Williams & Wilkins, Philadelphia, 1808-1811, 2003.	Publication
Martin, JE, LE Moores : Independent learning modules for pediatric neurosurgery. AANS/CNS Section of Pediatric Neurosurgery Annual Meeting, Phoenix AZ, 2002 December.	Presentation
Martin, JE, MK Rosner, C Neal, RR Moquin : Use of kyphotic titanium cages in the management of multilevel thoracic corpectomy: technical note (poster). International Meeting on Advanced Spine Techniques, Rome Italy, 2003 July.	Presentation
Martin, JE, MK Rosner, C Neal, RR Moquin : Use of kyphotic titanium cages in the management of multilevel thoracic corpectomy: technical note (poster). World Spine II International Conference, Chicago IL, 2003 August.	Presentation

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Martin, JE, MK Rosner, CJ Neal, RR Moquin : Use of Kyphotic Titanium Mesh Cages in the Management of Multilevel Thoracic Corpectomies (Poster). Southern Neurosurgical Society Annual Meeting, Orlando FL, 2003 March.	Presentation
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Martin, JE, RE Keating, PH Cogen, F Midgley : Long-term follow-up of direct heart shunts in the management of hydrocephalus. <i>Pediatr Neurosurg</i> , 38:94-97, 2003.	Publication
Monacci, W, J Ecklund : Neurosurgery and the War on Terrorism. <i>Neurosurgery News</i> , 4(1):1-2, 2003 Winter.	Publication
Moores, LE, JE Martin : Myelomeningocele and tethered cord: caring for an aging population. <i>Seminars in Neurosurgery</i> , 13:61-69, 2002 (FY03).	publication
Moquin, R, C Richardson, J Ecklund : Fused Deposition Modeling for Three Dimensional Evaluation of Spinal Deformities. International Meeting on Advanced Spine Techniques, Rome Italy, 2003 July.	Abstract
Moquin, R, C Richardson, M Rolli, J Ecklund : Evaluation of Spinal Deformities by Fused Deposition Models. Joint Section for Spinal and Peripheral Nerves of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons, Tampa FL, 2003 March.	Abstract
Moquin, R, C Richardson, M Rolli, W Yan, J Ecklund : Fused Deposition Modeling for Surgical Planning of Spinal Deformities. Joint Meeting of the North American and Japanese Spine Society, Maui HI, 2003 July.	Abstract
Moquin, R, R Hafez, J Ecklund : Spinal Tuberculosis. <i>Textbook of Neurological Surgery - Principles and Practice</i> , H Batjer, C Loftus (eds), Lippencott-Raven Publishers, Philadelphia, 4:3248-3253, 2003.	Publication
Moquin, R, S Parks, C Richardson, R Rice, P Matic, A Geltmacher, J Ecklund : Finite Element Analysis of the Spine Derived from Clinical Imaging Data. International Meeting on Advanced Spine Techniques, Rome Italy, 2003 July.	Abstract
Moquin, R, S Parks, C Richardson, R Rice, P Matic, A Geltmacher, J Ecklund : Finite Element Analysis of the Spine from Patient Specific Imaging Data. World Spine II International Conference, Chicago IL, 2003 August.	Abstract
Moquin, RR : Treatment of Thoracic and Lumbar Tumors. Anterior Spinal Surgery Workshop, Medtronic Sofamor Danek, Phoenix AZ, 2003 August.	Presentation
Moquin, RR : Treatment of Thoracic and Lumbar Tumors through the Anterior and Lateral Approach - Anterior Spinal Surgery Workshop. Spine Across the Sea Joint Meeting of the North American Spine Society and Japanese Spine Society, Maui HI, 2003 July.	Presentation
Moquin, RR : Paget's Disease of the Spine. <i>Textbook of Neurosurgery</i> , H Bather & C Loftus (eds), Lipencott-Raven, Philadelphia, 2003.	Publication
Moquin, RR, C Richardson, CJ Neal, JM Ecklund : Evaluation of Spinal Deformities by Fused Deposition Models (Poster). Joint Section for Spinal and Peripheral Nerve of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons, Tampa FL, 2003 March.	Presentation

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Moquin, RR, C Richardson, JM Ecklund : Fused Deposition Modeling for Evaluation of Spinal Deformities (Poster). Southern Neurosurgical Society Annual Meeting, Orlando FL, 2003 March.	Presentation
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Moquin, RR, DJ Geyer : Complete L5 Spondylectomy for Osteomyelitis Via Posterior Only Approach (Poster). International Meeting on Advanced Spine Techniques, Rome Italy, 2003 July.	Presentation
Moquin, RR, DW Polly, WR Klemme, W Monacci : Thoracic Hemivertebra Excision and Scoliosis Deformity Correction in Adults via a Posterior Only Approach (Poster). International Meeting on Advanced Spine Techniques, Rome Italy, 2003 July.	Presentation
Moquin, RR, J Ecklund : Tuberculosis of the Spine. Textbook of Neurosurgery, H Bather & C Loftus (eds), Lipencott-Raven, Philadelphia, 2003.	Publication
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Moquin, RR, S Parks, C Richardson, R Rice, P Matic, A Geltmacher, JM Ecklund : Finite Element Analysis of the Spine from Patient Specific Imaging Data (Poster). International Meeting on Advanced Spine Techniques, Rome Italy, 2003 July.	Presentation
Moquin, RR, S Parks, C Richardson, R Rice, P Matic, A Geltmacher, JM Ecklund : Finite Element Analysis of the Spine from Clinically Derived Imaging Data (Poster). Southern Neurosurgical Society Annual Meeting, Orlando FL, 2003 March.	Presentation
Moquin, RR, S Parks, C Richardson, R Rice, P Matic, A Geltmacher, JM Ecklund : Finite Element Analysis of the Spine from Patient Specific Imaging Data (Poster). World Spine II International Conference, Chicago IL, 2003 August.	Presentation
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Moquin, RR, W Monacci : Update on Neurosurgery and The War on Terrorism. Neurosurgery News, 4(2):, 2003 April.	Publication
Mulligan, L, J Ecklund, J Stockel : Radiographic Considerations in Spine Trauma. Textbook of Neurological Surgery - Principles and Practice, H Batjer, C Loftus (eds), Lippencott-Raven Publishers, Philadelphia, 2:1730-1736, 2003.	Publication
Polly, DW, MK Rosner, W Monacci, RR Moquin : Thoracic Hemivertebra Excision and Scoliosis Deformity Correction in Adults via a Posterior Only Approach. Neurosurgery Focus, 14(2):, 2003 February.	Publication
Salazar, A, P Cooper, J Ecklund : Neurological Disorders: Course and Treatment (2nd Ed). T Brandt, L Caplan, J Dickgans, C Diener, C Kennard (eds), Elsevier Science, New York, 765-781, 2002 (FY03).	Publication

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Warden, D, J Ecklund : The Effect of Concussion History on Cognitive Performance Following Acute Concussion. Annual Meeting of the American Academy of Neurology, HI, 2003 April.	Abstract
<b><u>Ophthalmology Service</u></b>	
Bishop, R, KS Bower, J Rabin : Comparison between induced higher order wave front aberrations following initial LASIK surgery and LASIK enhancement surgery. Invest Ophthalmol Vis Sci, 44:2610, 2003.	Abstract
Bower, KS : Sharp Anterior Segment Trauma. Tri-Service Ocular Trauma Course, Bethesda MD, 2003 May.	Presentation
Bower, KS : Sharp trauma of the anterior segment. Ophthalmic Care of the Combat Casualty, Thach AB, Ed. Textbook of Military Medicine, Borden Institute, 2003.	Publication
Chun, DW : Diabetic Retinopathy telemedicine study. Association for Research in Vision and Ophthalmology Conference, 2003.	Abstract
Cute, D, P Subramanian, B Warren, L Fannin, J Rabin, KS Bower : An evaluation of two different methods of marking the horizontal axis during excimer laser keratorefractive surgery for myopic astigmatism. Invest Ophthalmol Vis Sci, 44:2655, 2003.	Abstract
Dick, JSB : Endophthalmitis. Tri-Service Ocular Trauma Course, Bethesda MD, 2003 May.	Presentation
Dick, JSB : Vitreoretinal Complications - Surgical Management. Tri-Service Cataract Surgery Course, Bethesda MD, 2003 March.	Presentation
Eiseman, AS : Botulinum toxin A consent and patient expectations. George Washington University Ophthalmology Grand Rounds, Washington DC, 2002 November.	Presentation
Eiseman, AS : Evaluation of eyelid lesions and eyelid reconstructive techniques. Washington Oculoplastics Lecture Series, Washington DC, 2002 October.	Presentation
Eiseman, AS, JC Flanagan, A Brooks, E Mitchell, C Pemberton : Ocular surface, ocular adnexal, and lacrimal complications associated with the use of systemic 5-fluorouracil. Ophthal Plast Reconstr Surg, 19(3):216-224, 2003.	Publication
Fannin, LA : Cataract Management in the Glaucoma Patient. Tri-Service Cataract Surgery Course, Bethesda MD, 2003 March.	Presentation
Fannin, LA : Hyphema. Tri-Service Ocular Trauma Course, Bethesda MD, 2003 May.	Presentation
Fannin, LA : Small Pupils. Tri-Service Cataract Surgery Course, Bethesda MD, 2003 March.	Presentation
Fechter, HP : Malignant Glaucoma. Bascom Palmer Eye Institute Grand Rounds, 2003 May.	Presentation
Fechter, HP : Oral board preparation lecture. Brooke Ophthalmology Review Course, Fort Sam Houston TX, 2003 March.	Presentation
Fechter, HP : The Ocular Hypertension Treatment Study. Tri-Service Optometry Association, Bethesda National Naval Hospital, 2003 September.	Presentation
Fechter, HP : Trabeculectomy flag revisions. Bascom Palmer Eye Institute Grand Rounds, 2003 March.	Presentation

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Fechter, HP, NZ Gregori, D Miller, M Diaz, E Perez, D Anderson : Is it safe to go back in the water? A comparison of swimming water organisms and known pathogens. ASCRS National Meeting and Symposium on Cataract, IOL, and Refractive Surgery, San Francisco CA, 2003 April.	Presentation
Fechter, HP : Baerveldt Risk Factors. Bascom Palmer Eye Institute Residents' Days, 2003 June.	Presentation
Gregori, NZ, HP Fechter, D Miller, M Diaz, E Perez : A comparison of bacteria found in south Florida ocean and pool water with known ocular pathogens. Invest Ophthalmol Vis Sci, 44:1428, 2003.	Abstract
Hammond, MD, TP Ward, E Niemi, AS Eiseman : Adult orbital xanthogranuloma with adult onset asthma. Annual Meeting of the American Society of Ophthalmic Plastic and Reconstructive Surgeons, Orlando FL, 2002 October.	Presentation
Madigan, WP : Common Eye Problems in Children. USUHS Department of Pediatrics Grand Rounds, Bethesda MD, 2003 February.	Presentation
Madigan, WP : Congenital and Infantile Cataracts. Tri-Service Cataract Surgery Course, Bethesda MD, 2003 March.	Presentation
Madigan, WP : Horizontal and Vertical Strabismus. Washington Ophthalmic Residency Consortium (WORC), Washington DC, 2003 May.	Presentation
Mines, MJ : Post-operative management. Tri-Service Cataract Surgery Course, Bethesda MD, 2003 March.	Presentation
Mines, MJ : Terrorist Bombings. Tri-Service Ocular Trauma Course, Bethesda MD, 2003 May.	Presentation
Mines, MJ, KS Bower, TP Ward, AB Thach, DA Belyea, B Nelson : Robotic Microsurgical Repair of Corneal Lacerations in Rabbit Eyes. American Telemedicine Association 8th Annual Meeting, Orlando FL, 2003 April.	Presentation
Mines, MJ, KS Bower, TP Ward, AB Thach, KK Kramer, DA Belyea, B Nelson : Robotic microsurgical repair of corneal lacerations in rabbit eyes. Invest Ophthalmol Vis Sci, 44:907, 2003.	Abstract
Rimm, WR : Overview of Cataract Surgery. Tri-Service Cataract Surgery Course, Bethesda MD, 2003 March.	Presentation
Rocca, M, K Bower, J Pajak : Design and implementation of an electronic refractive surgery record. Telemed J, 9(1):S-69, 2003.	Publication
Simon, DP, AB Thach, KS Bower : Teleophthalmology in the evaluation of ocular trauma. Mil Med, 168(3):205-211, 2003 March.	Publication
Stutzman, RD : Anesthesia for Cataract Surgery. Tri-Service Cataract Surgery Course, Bethesda MD, 2003 March.	Presentation
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Subramanian, PS, B O'Kane, R Stefanik, J Stevens, J Rabin, RM Bauer, KS Bower : Visual performance with night vision goggles after photorefractive keratectomy for myopia. Ophthalmology, 110(3):525-530, 2003.	Publication
Subramanian, PS, JB Kerrison, PC Calvert, NR Miller : Orbital inflammatory disease after pamidronate treatment for metastatic prostate cancer. Arch Ophthalmol, 121(9):1335-1336, 2003.	Publication
Subramanian, PS, L Schramm, PN Hoffman : Electrical stimulation to enhance axonal regeneration after optic nerve injury. 29th Annual Meeting of the North American Neuro-Ophthalmology Society, Snowbird UT, 2003 February.	Presentation

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Thordsen, JE, B Warren, P Subramanian, KS Bower : Effect of brimonidine tartrate ophthalmic solution 0.15% on pupil diameter in normal eyes. Invest Ophthalmol Vis Sci, 44:792, 2003.	Abstract
Ward, TP : Current Status of the National and Military Smallpox Vaccination Programs and Cases of Ocular Vaccinia To Date. Bioterrorism and Disaster Preparedness, American Academy of Ophthalmology Mid-Year Forum, Washington DC, 2003 April.	Presentation
Ward, TP : Eye Care in the Theater of Operations - Army. Tri-Service Ocular Trauma Course, Bethesda MD, 2003 May.	Presentation
Ward, TP : Laser surgery of the posterior segment. Joint Commission of Allied Health Personnel in Ophthalmology Annual Continuing Medical Education Program for Ophthalmic Medical Personnel, Orlando FL, 2002 October.	Presentation
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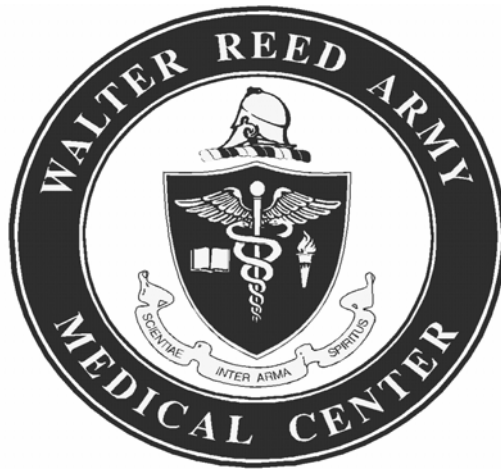
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**DEPARTMENT OF CLINICAL INVESTIGATION (DCI)**

# **ANNUAL RESEARCH PROGRESS REPORT**



## **FY 2003 VOLUME II**

**WALTER REED ARMY MEDICAL CENTER, WASHINGTON, DC**

## DETAIL SUMMARY SHEET

TITLE: Adrenal Suppression Following Short-Term Use of Corticosteroids: Results of a Prospective Study

KEYWORDS: Corticosteroids, adrenal suppression, low-dose ACTH stimulation test

PRINCIPAL INVESTIGATOR: O'Malley, Patrick MAJ MC

ASSOCIATES: Torrens, Javier MAJ MC; Sachar, David CPT MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: General Medicine

INITIAL APPROVAL DATE: 5 November 1997

### STUDY OBJECTIVE

To determine the presence and duration of measurable adrenal suppression following short-term, high dose prednisone therapy.

### TECHNICAL APPROACH

Prospective study of a convenience sample of patients being treated with short-term, high dose corticosteroid therapy. Participants will be tested for adrenal suppression using a low-dose ACTH stimulation test, at 1 week, and 4 weeks after completion of therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

30 patients (mean age: 56.3 years; range 21-85 yrs; 76% female) were enrolled. 56% were prescribed oral steroids for respiratory disease. One week after completion of steroid therapy, 92% of participants had competent adrenal responses, while 96% were adrenally competent at four weeks. The single patient with an inadequate response at 4 weeks had an adequate response at 1 week.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 30.

### CONCLUSIONS

Adrenal suppression after short course pulse steroids is probably short-lived and clinically insignificant beyond a few weeks.

## DETAIL SUMMARY SHEET

TITLE: Diagnostic Accuracy of Pleural Fluid Cholesterol and Lactate Dehydrogenase in Identifying Exudates vs. Transudates

KEYWORDS: pleural effusions, pleural cholesterol, pleural lactate dehydrogenase, exudates, transudates

PRINCIPAL INVESTIGATOR: CPT Jasmine T. Daniels MC

ASSOCIATES: Colin Daniels MD, William Kelly MD, Audrey Chang PhD, David Van Echo MD, Lisa Moores MD

DEPARTMENT: Medicine

STATUS: O

SERVICE: General Medicine

INITIAL APPROVAL DATE: 12 January 1999

### STUDY OBJECTIVE

To validate the results of Costa et al and evaluate the accuracy of Light's criteria in our population of patients. To determine if measurement of pleural fluid cholesterol in combination (paired or triple) with other pleural fluid measurement (LDH and protein) will provide similar or better sensitivity and/or specificity than Light's criteria (which uses serum and pleural fluid measurements) in differentiating exudative and transudative pleural effusions.

### TECHNICAL APPROACH

No new modifications. Follow-up at six months after diagnosis.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 2 and the total enrolled to date at WRAMC is 153. The last data analysis was performed after 100 patients were enrolled, and there is one pending at this time. There have been no adverse events related to this protocol.

### CONCLUSIONS

The initial data analysis suggests that the diagnostic accuracy of pleural fluid measures of LDH and cholesterol alone are approaching that of Light's criteria, and may ultimately be used in differentiating exudates and transudates. However, ongoing data collection continues.

## DETAIL SUMMARY SHEET

**TITLE:** Improving Rates of Acute Renal Allograft Rejection with a Regimen of Cyclosporin, Mycophenolate Mofetil and Prednisone

**KEYWORDS:** kidney transplantation, allograft rejection, allograft failure, cyclosporin, mycophenolate mofetil

**PRINCIPAL INVESTIGATOR:** Oliver, James LTC MC

**ASSOCIATES:** Abbott, Kevin LTC MC; Yuan, Christina LTC, MC; Welch, Paul COL, MC; Swanson, S. John LTC, MC; Reinmuth, Bruce

**DEPARTMENT:** Medicine

**SERVICE:** Nephrology

**STATUS:** C

**INITIAL APPROVAL DATE:** 29 May 1998

### STUDY OBJECTIVE

To describe the rates of rejection, graft and patient survival achieved in the WRAMC Renal Organ Transplant program as compared to national averages.

### TECHNICAL APPROACH

A retrospective review of transplant data from the WRAMC Organ Transplant database, from inpatient and outpatient charts being conducted in parallel with querying of the United States Renal Database System (USRDS). Rejection rates as a function of patient characteristics and of immunosuppressive regimen are being compared.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 132. The data has been mined and analyzed and five abstracts have been presented to the American Society of Nephrology and the National Medical Association annual meetings in 1999 and 2000.

### CONCLUSIONS

Transplant outcomes at WRAMC from 1992-1997 were improved from national data over the same time period. Racial differences between outcomes seen nationally were not seen at WRAMC. Introduction of mycophenolate mofetil and tacrolimus nationally appears to be resulting in some initial trends in improving outcomes.

## DETAIL SUMMARY SHEET

TITLE: The Impact of Therapeutic Plasma Exchange on the Medications Used in Transplantation

KEYWORDS: Plasmapheresis; Immunosuppression; Pharmacokinetics

PRINCIPAL INVESTIGATOR: Yuan, Christina M LTC MC

ASSOCIATES: Viola, Rebecca MPh

DEPARTMENT: Medicine

STATUS: O

SERVICE: Nephrology

INITIAL APPROVAL DATE: 19 January 1999

### STUDY OBJECTIVE

Prospective, descriptive study to document the clearance of various immunosuppressive drugs used in renal transplantation by plasmapheresis (TPE). Clearance of one of the following drugs will be assessed using pheresed plasma levels and plasma volume and patient plasma levels: daclizumab; mycophenolate mofetil; ganciclovir; cyclophosphamide; OKT3, and cytomegalovirus hyperimmune globulin.

### TECHNICAL APPROACH

Patients  $\geq 18$  years old undergoing plasmapheresis for various medical indications, and receiving any of the above medications will be asked to participate. Drug levels will be drawn peripherally prior to TPE, immediately post TPE, and at 2 and 4 hours post TPE. Levels will also be determined in the plasma effluent, and the volume of the effluent will be used to determine total clearance of drug. Levels will be determined at various laboratories. All data regarding clearance will be provided to the patient's physician, so that drug dosing and re-dosing may be done in accordance with the clearance data. Five patients will be entered, as opportunity presents itself. The diseases for which TPE is performed are rare, and the use of these drugs concurrently is also rare.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. No patients have been entered into the study in the past year. None have presented that met the inclusion criteria. The requirement for post-transplant plasmapheresis is a very rare occurrence in our small program - due to low incidence of post-transplant FSGS. We would like to keep the study open for five years pending the next case. (Closure of the study would be at the 2004 APR.)

### CONCLUSIONS:

None as yet.

## DETAIL SUMMARY SHEET

TITLE: Na<sup>+</sup>, K<sup>+</sup>-ATPase Inhibitor in the Mechanism of Hypertension in Diabetes Mellitus

KEYWORDS: diabetes; sodium pump inhibitor, ouabain

PRINCIPAL INVESTIGATOR: Yuan, Christina LTC MC

ASSOCIATES: Victor Bernet, MAJ, MC; Kevin Abbott, LTC, MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Nephrology

INITIAL APPROVAL DATE: 19 January 1999

### STUDY OBJECTIVE

To determine whether the presence of elevated levels of ouabain-like factor (OLF) is associated with diabetic nephropathy in Type I and Type II diabetics vs. diabetic patients without nephropathy.

### TECHNICAL APPROACH (Describe the methodology and note any modifications.)

Patients seen in the endocrine and nephrology clinics, with type I or type II diabetes, with or without nephropathy (as defined by presence of fixed proteinuria/albuminuria and hypertension) will be invited to participate in the study. A one time 10 cc sample of plasma and RBCs will be collected from a peripheral vein for determination of OLF levels. Levels will be measured in a blinded fashion. BP, weight, urine protein, serum creatinine, and glycosylated hemoglobin will also be determined. Patients must be  $\geq 18$  years or  $\leq 75$  years of age, not pregnant, not s/p kidney transplant, and with a serum creatinine of 1.5 mg% or less to be in the study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 3 and the total enrolled to date at WRAMC is 29. There have been no adverse events. There have been three quality control samples submitted. All clinical data has been collected. Measurement of sodium pump inhibitor has been completed in all 29 subjects. Vascular smooth muscle membrane potentials are in progress. Because of the death of one of the investigators at USUHS, and the serious illness of the PI at USUHS, accrual to the study was stopped in 8/2002, and is now permanently closed to accrual. Data analysis and vascular smooth muscle membrane potentials are in progress. This should be complete within several months, and any publication should be underway.

### CONCLUSIONS:

Of the 26 Type 2 diabetic subjects entered into the study, 16 had clinical nephropathy (PosNeph); 10 were without nephropathy (NegNeph) and had no microalbuminuria. Serum creatinine and glucose were the same between the two groups. MAP was not significantly different between the two groups ( $103 \pm 2$  vs.  $97 \pm 2$  mmHg,  $P = 0.119$ ), nor was hemoglobin A1C ( $7.6 \pm 0.4$  vs.  $7.0 \pm 0.4$ ,  $P = .0318$ ). 15/16 in the PosNeph group received an angiotensin converting enzyme inhibitor or receptor blocker vs. 6/10 in the NegNeph group. Plasma OLF inhibitor activity in PosNeph subjects was not significantly greater from that observed in NegNeph subjects ( $34.7 \pm 4.2\%$  vs.  $30.2 \pm 4.2\%$  NKA inhibition,  $P = 0.48$ ). Similarly, the activity of the Na<sup>+</sup>, K<sup>+</sup>-ATPase in the RBC membranes of PosNeph subjects was not significantly different from that of NegNeph subjects ( $0.307 \pm 0.04$  vs.  $0.272 \pm 0.01$   $\mu\text{mol Pi/mg membrane protein/hr}$ ,  $P = 0.45$ ). OLF inhibitor activity did not correlate with MAP, hemoglobin A1C, serum glucose, degree of proteinuria, or creatinine. In conclusion, in treated Type 2 diabetics, there were no significant differences in OLF inhibitor activity between subjects with clinical nephropathy and those without.

## DETAIL SUMMARY SHEET

TITLE: Patterns of Protein Size- and Charge-Selectivity in Clinical Kidney Disease

KEYWORDS: glomerulonephritis, proteinuria, permselectivity

PRINCIPAL INVESTIGATOR: LTC James D. Oliver MC

ASSOCIATES: Christina Yuan LTC MC; Paul Welch LTC MC; Sharda Sabnis MD; Maged Abdel-Rahim MS

DEPARTMENT: Medicine

SERVICE: Nephrology

STATUS: O

INITIAL APPROVAL DATE: 04 March 1999

### STUDY OBJECTIVE

To determine the fractional excretion of specific proteins in renal disease and controls, and to examine whether the patterns of proteinuria correlate with histological characteristics demonstrated on renal biopsy.

### TECHNICAL APPROACH

Patients seen in the nephrology clinic with kidney disease who are being referred for renal biopsy will have blood and urine samples drawn to measure the fractional excretions of various proteins:  $\beta$ -2 microglobulin, retinal binding protein, transferring, pancreatic and total amylase, IgG and IgG4, and albumin polymers. These will be compared to values obtained from a matched set of health control volunteers. From the biopsy specimens, the essential diagnostic category and grading of the severity of disease will be determined in a blinded fashion. The fractional excretions will be correlated to the histological changes. Patients must be over 18 years of age and not s/p kidney transplant to be eligible.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

To date we have obtained assays for retinol binding protein,  $\beta_2$  microglobulin, and IgG. These assays have been calibrated and their sensitivities verified. We have identified commercial assays available for albumin, transferrin, and pancreatic amylase and will be obtaining them and performing the necessary calibration experiments on them in the upcoming months. We have assembled supplies for developing our own ELISA assays for amylase and are currently working to complete this. We anticipate patient enrollment beginning Spring 2003.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

None to date.



## DETAIL SUMMARY SHEET

**TITLE:** The Utility of Electron Beam Computed Tomography (EBCT) as a Screening Test for Coronary Artery Disease and as an Intervention for Risk Factor Modification Among Over 40 Active Duty Personnel

**KEYWORDS:** Coronary artery disease, risk factors, prognosis, computed tomography

**PRINCIPAL INVESTIGATOR:** Taylor, Allen LTC MC

**ASSOCIATES:** O'Malley, Patrick MAJ MC; Jones David LTC MC; Vernalis, Marina COL MC; Feuerstein, I; Brazaitis, M COL MC

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Cardiology

**INITIAL APPROVAL DATE:** 25 November 1997

### STUDY OBJECTIVE

To evaluate the prevalence, relationship to coronary risk factors, management impact and prognosis of coronary calcium detected using electron beam computed tomography in active duty Army personnel.

### TECHNICAL APPROACH

- A. 2000 consecutive, over age 40 active duty Army personnel from the National Capital Area will be screened for conventional coronary risk factors and electron beam computed tomography. This cohort will be followed annually for the occurrence of cardiovascular events.
- B. 450 of the participants will be enrolled in a randomized controlled trial (2x2 factorial design) comparing immediate vs. deferred EBCT results and standard care vs. case management risk factor modification.

### PRIOR AND CURRENT PROGRESS

Recent literature continues to support the continuation of the current study protocol. The primary aim of this study, to compare EBCT and the Framingham index for their prognostic utility in coronary heart disease, remains unanswered within the current literature. As of 5 September 2002, 1840 participants have been enrolled in the cohort study (277 since last APR). The randomized trial cohort follow-up was completed in March 2002. The final goal of the study is to enroll 2000 participants. A total of ten adverse events have been reported. None were directly related to participation in the study. The contract to SAR Inc. was renewed through MRMC as of August 2001 and is continuing. Funding is still through a CDMRP grant and a parallel MRMC human subject review process is proceeding. Per DCI and the OHRP report, we no longer collect any demographic data on individuals who decline participation in the project. The following amendments to the protocol have been completed in the last year:

1. A serologic study of banked specimens to evaluate HDL kinetics.
2. A request to use the ICDB to find eligible participants for direct mail advertisement.

### CONCLUSIONS:

Enrollment in the cohort study is nearing completion. Analysis of the randomized trial is actively underway. Continued subgroup analyses on questions of interest within the approved data set are continuing.

## DETAIL SUMMARY SHEET

**TITLE:** Assessment of Clinical Outcome Using Prothrombin Time Patient Self Testing (PST) to Monitor Long Term Anticoagulation Therapy

**PRINCIPAL INVESTIGATOR:** Calagan, Jennifer L. LTC MC

**ASSOCIATES:** Thomas, Susan CRNP, John, Cheryl RN; Vernalis, Marina COL MC

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Cardiology

**INITIAL APPROVAL DATE:** 16 June 1998

### STUDY OBJECTIVE

To assess the use of Patient Self-Testing (PST) to monitor the effect of Coumadin® therapy for effectiveness, safety and convenience/compliance. To assess the use of HealthBuddy® telephone/internet communication device to monitor further complications, status and Coumadin® use in WRAMC Coumadin® Clinic patients. Additionally, to compare the use of PST and HealthBuddy® to standard/traditional in-hospital monitoring of effects of Coumadin® therapy.

### TECHNICAL APPROACH

PST has been conducted using the ProTime® Microcoagulation System (ITC, Edison, NJ). An initial group of patients was advised of the protocol, trained in the use of the system, and then randomized to either standard monitoring or the PST arm. The member of the second group was further trained on the use of the system, given supplies and tracking forms, and issued a home unit. Patients in the first/control group will remain under the standard clinic protocol for monitoring of PT/INR, but will be also trained in and given report and tracking forms. The outcomes studied will be percentage of time within therapeutic range, precision in dose adjustment, patient compliance, complications and patient satisfaction. After this study was started, funding and the technology to monitor patient health status, Coumadin® use, potential complications and other relevant changes to medical regimen became available in the form of the HealthBuddy®, a device which allows two-way non-simultaneous exchange of information between Coumadin® Clinic and the patient at home. The device plugs into an existing phone line and is programmed to communicate via the Internet with a server that can post the responses to a secure, pass-worded web site. This should allow patients and Coumadin® Clinic to exchanges questions and information without a patient visit on-site or a series of phone calls. This device has been used with other medical conditions (e.g. diabetes) but never tested for use in a high volume clinic with military population on fairly high-risk therapy. The need for prompt detection of aberrancies in INR, patient's medical condition, or new or deleted medications suggest that such a device might improve efficacy of therapy while reducing potential for complications or earlier detection of complications. The protocol was amended to include four arms: the original two (control and PST), a HealthBuddy® arm, and an arm with both devices. It also included subgroups of "new" patients in the study groups. An additional control group 1A, which consisted of enrolled patients who could not or did not want to use the ProTime® or Health Buddy® devices, was generated. Enrollment was halted after February 2002, and patients continued to be followed with data collection for one year each.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 155. Amendments/Modifications: None further.

Adverse Events in study patients cumulative: Major: (not felt to be related to study, expected in this population, not counseled in Consent form). Death (4).

### CONCLUSIONS

Study stopped new enrollment 28 February 2002 based on time needed to complete follow-up and budget remaining. Target enrollment was not met. Patients were each followed for one year with follow-up of the last enrolled patient completed in February 2003. Study patients continue to be followed by the WRAMC Anticoagulation Management Service (Coumadin Clinic). Data available on patient acceptance of the two technologies was assessed in May of 2002 with preliminary data presented at the 2002 Annual Meeting of the American Telemedicine Association.. This data indicates that inability to use ProTime® device to standard and dissatisfaction with either the ProTime® or the

Health Buddy® caused withdrawals or change of arm to control group treatment. Dissatisfaction with not being assigned to a ProTime® group also caused withdrawals. Some withdrawals were due to discontinuation of Coumadin® therapy by PCP or specialist.

Adverse events accumulated at approximately the same rate as the prior year, occurred in different study groups, and do not appear to be related to the study methods. The majority of events were likely complications of underlying conditions, and others were at least associated with the use of an anticoagulant (bleeding complications). Adverse outcomes in study patients were consistent with those expected in a similar population based on natural history data.

## DETAIL SUMMARY SHEET

TITLE: Non-Invasive Coronary Artery Disease Reversal

KEYWORDS: Heart Disease Reversal; Lifestyle Modification; Coronary Artery Disease

PRINCIPAL INVESTIGATOR: Vernalis, Marina COL MC

ASSOCIATES: Ocuin, Esther LTC MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Cardiology

INITIAL APPROVAL DATE: 21 September 1999

### STUDY OBJECTIVE

The overall purpose of this study is to determine if comprehensive lifestyle changes (low-fat vegan diet supplemented with soy and antioxidants, moderate aerobic exercise, stress management, and group support) can slow, stop or reverse the progress of coronary artery disease. Specific objectives are as follows:

1. To investigate the efficacy of intensive lifestyle modification in improving the clinical status of patients with moderate to severe coronary artery disease (CAD) measured by a 50% reduction in angina frequency. Secondary endpoints to this objective will measure New York Heart Association (NYHA) class and exercise time.
2. To investigate the effect of intensive lifestyle modification on levels of CAD associated "markers" (such as lipids, homocysteine, C-reactive protein and fibrinogen) via development and analysis of study data banks.
3. To investigate the effect of intensive lifestyle modification on measurements of established CAD (such as exercise tolerance, NYHA functional class, angina, blood pressure and weight).
4. To determine if a disciplined military active duty and retired patient population can achieve and adhere to the goals of this lifestyle change program in a non-residential, outpatient setting. This will be determined using patient questionnaires addressing degrees of observance of the program's components.
5. To determine the potential effects of the program on DoD healthcare expenditures for CAD treatment.
6. To establish a sera bank for possible future research of markers as yet unidentified.

### TECHNICAL APPROACH

A. Study Design - This ongoing study is designed as a prospective, non-randomized, single-arm (treatment), observational trial, in which each individual serves as his/her own control, comparing outcomes to baseline data. The Non-Invasive Coronary Artery Disease Reversal protocol received final approval by the WRAMC DCI on 21 September 1999. Required revisions were received on 28 January 2000.

B. Study Addenda – There have been no study addenda since the last review.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 33 and the total enrolled to date at WRAMC is 169. Fifty-four have completed the one-year program and 59 are actively participating in the maintenance program. Thirty-four participants (20% dropout rate) have either voluntarily withdrawn or have been medically withdrawn from this study (see table).

Reason for Withdrawal	Count
Death	1
Lack of Commitment to Program	23
Deployment/Separation from Active Duty/Reassignment	5
Chronic medical condition deterioration	4
Seek other treatment options	1

Work Unit # 1224-99 [Continued]

Participants span the age spectrum of 31 to 81 years old with a mean age of 59.7 years (SD=9.9), 31% are female, and 22% are from minority groups. Sixty-six percent have documented coronary artery disease (CAD). Of those with CAD, 82% have had at least one revascularization procedure (bypass surgery or angioplasty). Additionally, 63% of the participants suffer from hypertension, 17% with diabetes and 73% are taking cholesterol-lowering medications. Of the enrolled participants, 32 are active duty, 99 are from the retired ranks, 37 are eligible family members and one is a Secretary of Defense designee.

Adverse events related to subjects

There has been one serious adverse event in the course of this study. Participant died as a result of a massive right hemisphere hemorrhagic CVA. The table below summarizes the adverse events as either cardiac or non-cardiac. All adverse events (Death, ER visits, hospitalizations, etc) have been submitted to WRAMC Department of Clinical Investigations (DCI) for review. Changes have been made to the consent form as a result of several adverse events. These changes have been discussed in previous annual reports.

<u>Adverse Event Summary</u>	<u>Number of Episodes</u>
Death	1
Cardiac related hospitalizations/ER visits/Cardiac Catheterizations with or without interventions	51
Non-cardiac related hospitalization/ER visits	62

CONCLUSIONS

A. Preliminary Baseline vs. 12 Weeks Clinical Data (Paired t-tests)

Changes in Exercise Capacity					
	N	Baseline	12 Weeks	% Change	P-value
Minutes	121	8:55	10:05	+13.1%	.0005
METS	121	9.3	10.8	+16.1%	.0005

Changes in Risk Factors					
	N	Baseline	12 Weeks	% Change	P-value
Weight	132	199.8	186.6	-6.6%	.0005
Body Fat	130	28.4	26.0	-8.5%	.0005
Systolic BP	132	129.7	123.2	-5%	.0005
Diastolic BP	132	74.0	71.1	-3.9%	.0005
Total Cholesterol	132	178.7	155.5	-13%	.0005
HDL	132	49.7	41.9	-15.7%	.0005
LDL	132	103.7	87.3	-15.8%	.0005
Triglycerides	132	158.8	173.8	+9.4%	NS
C-reactive protein	132	0.346	0.292	-15.6%	NS
Lipoprotein-a	132	39.3	41.4	+5.3	NS
Homocysteine	132	9.6	9.1	-5.2%	.025
Fibrinogen	132	387.8	398.3	+2.7%	NS

Changes in SF 36 Survey Composite Scores					
	N	Baseline	12 Weeks	% Change	P-value
Physical Composite Score	130	44.95	46.98	+4.5%	.002
Mental Composite Score	130	53.07	54.81	+3.3%	.035

Work Unit # 1224-99 [Continued]

Changes in Mental Health Survey Scores					
	N	Baseline	12 Weeks	% Change	P-value
Perceived Stress Scale	129	11.34	9.23	-18.6%	.0005
Center for Epidemiological Studies Depression Scale	129	7.59	6.62	-12.8%	NS
Cook Medley Hostility Scale	129	7.16	6.62	-7.5%	NS

B. Preliminary Baseline vs. One Year Clinical Data (Paired t-tests)

Changes in Exercise Capacity					
	N	Baseline	1 Year	% Change	P-value
Minutes	82	8:58	10:11	+13.6%	.0005
METS	82	9.2	10.7	+16.3%	.0005

Changes in Risk Factors					
	N	Baseline	1 Year	% Change	P-value
Weight	90	191.7	183	-4.5%	.0005
Body Fat	87	28.1	25.6	-8.9%	.0005
Systolic BP	91	132.0	124.4	-5.8%	.0005
Diastolic BP	91	74.4	70.5	-5.2%	.001
Total Cholesterol	91	182.8	179.0	-2.1%	NS
HDL	91	50.1	47.3	-5.6%	.001
LDL	91	107.6	99.9	-7.2%	.001
Triglycerides	91	175.0	187.3	+7%	NS
C-reactive protein	91	.317	.263	-17%	NS
Lipoprotein-a	91	39.6	39.8	+1%	NS
Homocysteine	91	10.0	8.7	-13%	.0005
Fibrinogen	91	389.9	372.6	-4.4%	.001

Changes in SF 36 Survey Composite Scores					
	N	Baseline	1 Year	% Change	P-value
Physical Composite Score	89	44.37	47.56	+7.2%	.001
Mental Composite Score	89	53.88	55.23	+2.5%	NS

Changes in Mental Health Survey Scores					
	N	Baseline	1 Year	% Change	P-value
Perceived Stress Scale	87	10.56	8.13	-23%	.001
Center for Epidemiological Studies Depression Scale	89	7.22	5.52	-23.5%	.016
Cook Medley Hostility Scale	89	6.85	5.76	-15.9%	.006

Work Unit # 1224-99 [Continued]

Program Adherence (Cohorts 1-6)\*

	Phase 1	Phase 2	Phase 3	Overall
Diet (%)	92.3	92.0	90.2	91.7
Aerobic Exercise (%)**	60.9	56.4	47.9	57.2
Days/Wk	2.8	2.6	2.2	2.6
Min/Wk	109.7	101.5	86.2	102.9
Nonaerobic Exercise	-	-	-	-
Days/Wk	2.6	2.3	2.3	2.3
Min/Wk	110.4	114.0	135.5	113.2
Stress Management (%)	75.1	73.8	66.0	71.1
Days/Wk	5.6	5.5	5.0	5.3
Min/Wk	297.6	288.2	253.4	277.7

\*Data from patients completing  $\geq 70\%$  of required personal adherence logs.

\*\*Data from Cohort 1-5.

Dietary analysis based on adherence to required food patterns/frequencies.

Both aerobic (exercise in target heart rate) and non-aerobic exercise has been measured. Participants exercise for an average of 3.6 hours per week during. Treadmill exercise testing data is available on 121 participants who have completed the program. Preliminary results show that over 50% of the total exercise time is attributable to non-aerobic exercise. Despite the latter, a significant improvement in treadmill exercise time since enrollment and suggests the duration and not necessarily the type of activity plays a role in the sustainment of the improved function. This is coupled with a significant overall improvement in cardiovascular fitness as defined by METS (metabolic equivalent). After 3 months, patients increased their fitness level by 1.5 METS. Twelve-month preliminary data shows sustainment of both exercise time and workload at a significant level. There is evidence-based data that an increase of 1-MET in functional capacity may convey a 12% increase in survival.

Functional health improvement has also been validated in this population through the use of the Health Status Survey (SF-36), which is a widely used tool for measuring health status and outcomes. As seen in the above table, improvements have been seen in both the physical and mental components of this tool.

The overall mean compliance with the plant-based vegetarian dietary guidelines after 12 months of participation is 92 %. Participants have done remarkably well in integrating this ultra-low fat diet into their daily routine. Reductions in weight and body fat have also been seen as a result of the diet. The average weight loss at 12 weeks is 13 pounds with almost 3% reduction in body fat and seems to hold steady at one year.

After 3 months, there is a reduction in lipid profiles in both patients on and off statin therapy. Triglycerides show a 9% increase at the same time point. The decrease in HDL and increase in triglycerides are similar to the findings of Dr. Dean Ornish in both his initial Lifestyle Heart Trial as well as the Multicenter Lifestyle Demonstration Project. Although the Lifestyle Heart Trial showed plaque regression, there appears to be competing effects of the program on the HDL and triglycerides. The importance of the latter is not clear and needs further clarification possibly through lipoprotein kinetics. Lipid profiles show more modest improvements at one year.

Overall stress management adherence is highest during the first 12 weeks (75% or 45 minutes/day) and decreases to 40 minutes/day at 12 months. Despite difficulty integrating this component into their daily routines, reduction in stress as measured by the Perceived Stress Scale (PSS) is significant at both 3 month and 12 month time periods. At one year, there are also significant improvements in both the depression and hostility scales.

The preliminary short-term results from this study are impressive by way of physiologic and emotional measures. These changes argue well for being able to demonstrate long-term success with respect to more definitive outcomes such as adverse clinical CV events including hospitalization for an acute coronary syndrome or the need for future coronary revascularization procedures. In addition, the effects of the core components on carotid intima media thickness (CIMT), a validated measure of atherosclerosis burden, will shed important information on the regression or stabilization of plaque. Results of the CIMTs from these subjects are not yet available.

Work Unit # 1224-99 [Continued]

Preliminary analysis has been done on several subsets of subjects. In 99 patients (35 females; 68% with coronary artery disease), baseline and 3-month scores on The Health Status Survey (SF-36), Perceived Stress Scale (PSS), Cook-Medley Hostility Scale (CMHS) and The Center for Epidemiological Studies-Depression Scale (CES-D) were compared by gender using the paired-sample t test statistic. Adherence for stress management (72%) and group support (75%) did not differ between groups. Males showed significant improvement on the mental composite score of the SF-36 ( $p=.049$ ) and the PSS ( $p=.001$ ). Improvements in both the CMHS and CES-D scores for males approached significance. There was a trend toward improvement in females on all scales. After three months, the psychosocial techniques practiced in this model seem to benefit men more than women. This data suggests a gender difference response. Long-term observation is needed to confirm these results. It is possible that effective psychosocial interventions are gender specific.

In 123 patients (mean age 60 yrs, 22 diabetics) significant changes in fasting glucose and lipid levels are shown. Adherence to the diet was greater than 70% for all patients. After 3 months, total, LDL and HDL cholesterol were significantly ( $p<0.008$ ) reduced in both groups. Triglycerides were significantly increased only in diabetics ( $p=0.031$ ). Fasting glucose was reduced within the diabetic group showing a trend toward significance ( $p=0.065$ ). Compared to non-diabetic patients, diabetics showed a significantly ( $p=0.021$ ) greater decrease in fasting glucose from baseline to 3 months. All parameters of lipid metabolism were not significantly different in diabetics compared to non-diabetics. Values in Table are means  $\pm$  Standard Deviation. While diabetics showed similar responses in lipid metabolism when compared to non-diabetics, they also showed modest improvements in glucose control. Contrary to current guidelines, diabetics may lower their cardiovascular risk with an ultra low-fat, high carbohydrate diet.

Changes from 0 to 3 months

(mg/dL)	Diabetics (n=22)	Non-diabetics (n=101)
<u>Fasting Glucose</u>	-16 $\pm$ 40	-3 $\pm$ 9
Total Cholesterol	-15 $\pm$ 24	-22 $\pm$ 33
HDL	-6 $\pm$ 8	-8 $\pm$ 14
LDL	-11 $\pm$ 18	-16 $\pm$ 23
TG	30 $\pm$ 61	12 $\pm$ 101

In 123 patients (2/3 with CAD; mean age: 60 years) who reached the 3-month milestone, 88 were on statin therapy with no significant change in dose. Overall program adherence was  $>70\%$ . At 3 months, each group had significant ( $p<.0005$ ) decreases from baseline in total, LDL, and HDL cholesterol but there was no difference between groups. Triglycerides were also not different between groups but increased significantly from baseline ( $p=0.026$ ) in the on-statin group. Values in Table: Mean  $\pm$  Standard Error. Other significant improvements (baseline-3 months,  $p<.0005$ ) in both groups included: Fitness in METS (Statin: 1.5  $\pm$  0.2; No Statin: 1.7  $\pm$  0.3), % Body Fat (Statin: -2.4  $\pm$  0.3; No Statin: -2.8  $\pm$  0.7), Waist Circumference Inches (Statin: -1.4  $\pm$  0.2; No Statin: -1.7  $\pm$  1.4), BMI (Statin: -1.9  $\pm$  0.1; No Statin: -2.1  $\pm$  1.3). Patients on statin therapy achieve further benefit in lipids with intensive lifestyle change and also demonstrate benefits in fitness and body composition that cannot be attained with statin therapy alone. For optimal management of cardiovascular risk, even patients on statin therapy should be encouraged to pursue lifestyle change.

Lipid Changes (0-3 months), mg/dL

	Statin	No Statin
Total Cholesterol	-19 $\pm$ 3	-27 $\pm$ 5
LDL	-15 $\pm$ 2	-14 $\pm$ 5
HDL	-6 $\pm$ 0.9	-11 $\pm$ 4
TG	21 $\pm$ 11	1 $\pm$ 14

In 157 (98 men, 49women) enrolled patients (mean age: 60yrs; % with CAD: 66), baseline CRP was significantly higher in women than men: 1.7 (0.9,3.8) vs. 2.8 (1.3,6.0),  $p=0.015$ . One-year data is reported in 81 patients (55 men,



Work Unit # 1224-99 [Continued]

28 women) who have completed the program. Adherence was > 70% in all program components. At one year, CRP in men did not change, while women showed a significant CRP decrease:

	CRP Changes Over One Year		p
	Baseline	One Year	
Men	1.2 (0.8, 2.5)	1.5 (0.7, 2.9)	0.557
Women	3.1 (2.0, 7.0)	2.1 (1.0, 4.6)	0.025

Intensive lifestyle intervention appears to affect CRP favorably in women but not in men. These CRP changes cannot be attributed to a specific program component and may be related to factors such as weight loss and/or LDL cholesterol levels. Furthermore, use of CRP levels to predict of efficacy of an intervention on long-term cardiovascular outcomes may require attention to gender differences.

The program has the potential to operationalize bench research and to identify what is clinically applicable not only to the military population but the general population. Future goals include a randomized, prospective study to tease out the relevance of the core components especially as it relates to psychosocial interventions. It will also be important to identify the additive effects of lifestyle modification to pharmacoprevention of atherosclerotic cardiovascular disease.

## DETAIL SUMMARY SHEET

TITLE: Establishment of a Thyroid Patient Serum Bank

KEYWORDS:

PRINCIPAL INVESTIGATOR: Burch, Henry LTC MC.

ASSOCIATES:

DEPARTMENT: Medicine

SERVICE: Endocrine

STATUS: C

INITIAL APPROVAL DATE: 21 April 1998

### STUDY OBJECTIVE

To collect serum from a variety of patients with endocrine disorders to facilitate future research requiring serum.

### TECHNICAL APPROACH

Obtain informed consent. Perform standard phlebotomy, centrifuge, and store specimens at -70° C.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 158.

### CONCLUSIONS

The serum bank has been inactive since the retirement of Dr. Barbara Solomon. It will be discontinued and existing samples will be destroyed.

## DETAIL SUMMARY SHEET

TITLE: Establishment of a Thyroid Tissue Bank

KEYWORDS:

PRINCIPAL INVESTIGATOR: Burch, Henry COL MC.

(Bernet, Victor LTC MC is assuming PI responsibilities. Paperwork has been submitted)

ASSOCIATES:

DEPARTMENT: Medicine

SERVICE: Endocrine

STATUS: O

INITIAL APPROVAL DATE: 21 April 1998

### STUDY OBJECTIVE

To create and maintain a tissue and fine needle aspiration bank from patients with a variety of thyroid disorders, in order to facilitate future research projects requiring thyroid tissue.

### TECHNICAL APPROACH

After obtaining informed consent, a small piece of tissue being removed for clinical indications is snap frozen in liquid nitrogen and stored in a -70 C freezer.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Surgical thyroid tissue continues to be collected for the thyroid tissue bank. There have been no adverse events associated with participation in this protocol.

The number of subjects enrolled to the study since last APR at WRAMC is 41 and the total enrolled to date at WRAMC is 156.

### CONCLUSIONS

None.

## DETAIL SUMMARY SHEET

**TITLE:** Short Segment Barrett's Esophagus: Prevalence, Clinical Characteristics, and Responses to Long-Term Antisecretory Therapy

**KEYWORDS:** short segment, Barrett's Esophagus, Prilosec

**PRINCIPAL INVESTIGATOR:** Wong, Roy K.H. COL MC

**ASSOCIATES:** Maydonovitch CL

**DEPARTMENT:** Medicine

**SERVICE:** Gastroenterology

**STATUS:** O

**INITIAL APPROVAL DATE:** 29 November 1994

### STUDY OBJECTIVE

To determine: 1) the prevalence of Short-Segment Barrett's Esophagus (SSBE) in patients undergoing upper endoscopy in WRAMC's Gastroenterology Clinic; 2) the response of SSBE to maximal antireflux therapy with Prilosec; 3) the incidence of specialized intestinal metaplasia of the esophagus in a cohort of patients originally identified in part I; and 4) the 24hr pH and esophageal manometry characteristics of patients with specialized intestinal metaplasia of the gastroesophageal junction (EGJSIM).

### TECHNICAL APPROACH

This has been two-part study with several addenda to allow further study. In Part I, patients complete a questionnaire prior to endoscopy (EGD). During the patient's routine EGD, photographs and four biopsies of the distal esophagus will be obtained to evaluate the presence of SSBE. In Part II, patients found to have SSBE undergo repeat EGD with biopsy, manometry, and 24-hour pH prior to treatment with Prilosec and are then followed at 3-month intervals for 2 years. In the follow-up phase to Part I, 151 patients found to have specialized intestinal metaplasia (SIM) of the esophagus (at the EGJ, SSBE and LSBE) in part I are asked to return for repeat surveillance biopsies to assess the incidence of SIM in this cohort. The most recent addendum /exception to DCI policy (October 2000) granted approval to continue long-term follow up patients identified with SIM and to perform manometry/ pH studies on the cohort of 45 patients with EGJSIM.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been no new enrollment since the last APR. COL Roy Wong has been designated the new PI as Dr. Cumings has been transferred to Madigan AMC. This study is remaining open to continue long-term follow studies on the cohort of 150 Barrett's patients identified out of 889 patients studied under Part I of the study. No new patients will be enrolled in this study

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC in Phase 1 of the study is 889 patients undergoing routine EGD.

### CONCLUSIONS

Long-segment Barrett's esophagus patients defined as having a >3cm length BE segment tend to be Caucasian males. These patients have greater degrees of esophageal acid reflux than patients with Short-segment ( $\leq 3$ cm) Barrett's esophagus or EGJ\_SIM (specialized intestinal metaplasia at the EG junction).

## DETAIL SUMMARY SHEET

TITLE: Hypnosis for the Treatment of Upright Gastro-Esophageal Reflux

KEYWORDS: Upright Reflux

PRINCIPAL INVESTIGATOR: Cumings, Mark MAJ MC

ASSOCIATES: Roy Wong COL MC, Dr. Harold Wain, Corrinne Maydonovitch

DEPARTMENT: Medicine

STATUS: O

SERVICE: Gastroenterology

INITIAL APPROVAL DATE: 28 April 1998

### STUDY OBJECTIVE

- A) To study the efficacy of hypnosis versus omeprazole in the treatment of upright reflux
- B) To determine the prevalence and types of psychiatric abnormalities in patients with upright reflux
- C) To characterize the pathophysiology of successful treatment in patients undergoing hypnosis

### TECHNICAL APPROACH

Addendum: The prospective arms of the trial were terminated due to poor enrollment in that phase with an appropriate adjustment of the title. A psychiatric questionnaire (PRIME-MD) was added to streamline psychiatric assessment. Patients are now offered self-hypnosis, with a psychiatric evaluation to determine hypnosis capacity, as a "pilot-study"-like format with repeat pH measurement and gastric emptying at 8 weeks after starting the self-hypnosis.

Current Approach: Those patients identified to have upright reflux by symptom pattern would undergo 24-hr pH testing to confirm upright reflux. Those found to have upright reflux on clinically ordered pH tests would also be offered enrollment in the study. A validated psychiatric questionnaire, Prime-MD-II, will be completed and a gastric emptying study will be completed. All subjects will be offered self-hypnosis training in conjunction with the routine medical therapy they were receiving prior to study enrollment. After 8 weeks, the subjects doing self-hypnosis will be asked to return for a repeat 24-hr pH test off medications, but while using self-hypnosis. They would be asked to get another gastric emptying study using self-hypnosis to quantify any potential differences in gastric emptying using self-hypnosis versus the previously attained baseline gastric emptying study. The use of a "partial study", with those patients unwilling to try self-hypnosis still having the validated psychiatric questionnaire and gastric emptying study, would be continued. Patients who completed the study prior to the recent addendum are being contacted, re-consented and are completing the psychiatric questionnaire to complete our database.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been no new data in the literature concerning this area. No modifications/addenda have been made to the study plan since the last APR. No new pts have been enrolled since the last APR. There have been no adverse events or withdrawals. Given the lack of enrollment and the transfer of the Principal investigator to Madigan AMC, the study is being closed.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 23. The total number enrolled study-wide is 23, if multi-site study.

### CONCLUSIONS

Gastric emptying can vary from rapid to delayed in patients with upright reflux. The pattern of gastric emptying does not seem to play a significant role in the severity of upright reflux.

## DETAIL SUMMARY SHEET

TITLE: Long-Term Prevention of Recurrent Peptic Ulcer Hemorrhage in Patients Infected with *Helicobacter Pylori*: A Multi-Center, NIH-Funded, Prospective, Randomized Double-Blind Study

KEYWORDS:

PRINCIPAL INVESTIGATOR: Wong, Roy COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Gastroenterology

STATUS: C  
INITIAL APPROVAL DATE: 23 March 1999

### STUDY OBJECTIVE

The objectives of this study are:

- 1) To determine the efficacy and safety of *H.pylori* eradication alone versus *H.pylori* eradication combined with daily full dose H2RA in preventing recurrences of duodenal ulcer and gastric ulcer hemorrhage
- 2) To document whether recurrences of ulcer hemorrhage are associated with NSAIDS-ASA and/or *H.pylori* recurrence of *H. pylori* infection

### TECHNICAL APPROACH

Patients diagnosed within six months with DU or GU hemorrhage with *H.pylori* infection may enter the study at either phase I or phase II. *H.pylori* infection will be documented using CLO, ELISA, histopathology and/or C13 breath test. In phase I, study patients will receive ten days of antimicrobial therapy for *H.pylori* eradication. Eradication will be documented by C13 urea breath test at least six weeks after completion of antimicrobial therapy. Those in whom eradication is successfully achieved will be randomized to the H2RA vs. placebo in a double-blind fashion. Patients whose *H.pylori* was not eradicated by two courses of antimicrobial therapy or diagnosed with greater than/equal to five gastric and/or duodenal erosions after *H.pylori* eradication will receive full-dose H2RA and will also be followed up long term as a comparator group. All patients in Phase II will be followed-up long-term for a median of 36 months. The follow-up entails an interview of their symptoms associated with GU and/or other health, changes in health status and direct and indirect costs associated to health reasons. Enrollment is closed for this study.

### PRIOR AND CURRENT PROGRESS

There are a total of 341 patients randomized from 27 study sites - 175 to H2RA and 171 to placebo. Seventeen patients are from WRAMC. 126 patients withdrew from the study and three of these were from WRAMC. There are a total of 346 adverse events reported. Of those reported, 11 were from WRAMC and they were non-serious and unrelated to the study. There have been no major complications or drug related adverse events. There are three abstracts submitted to DDW 2003 from this research study.

### CONCLUSIONS

This study supports the hypothesis that *H.pylori* eradication in ulcer patients may increase the incidence of erosive esophagitis during long-term follow-up. The overall incidence of erosive esophagitis in the placebo group was 10.9%. Daily full dose H2RA was associated with a significantly lower incidence of erosive esophagitis in patients with ulcer hemorrhage who had *H.pylori* eradicated. Supported by NIH DK49527.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9633 - A Phase III Study of Adjuvant Chemotherapy After Resection for Patients with T2NO Stage I NON-Small Cell Carcinoma of the Lung

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 05 November 1997

### STUDY OBJECTIVE

To determine if adjuvant chemotherapy can favorably alter the prognosis for high-risk patients with T2NO NSC carcinoma of the lung. To compare failure-free survival of these patients who have and have not received adjuvant chemotherapy after surgical resection. To determine toxicity associated with adjuvant chemotherapy, and to describe pattern of recurrence.

### TECHNICAL APPROACH

Eligible patients with T2NO NSC carcinoma of the lung will be randomized after surgical resection to receive standard therapy - observation or to receive adjuvant chemotherapy with taxol and carboplatin. Chemo will be given in hematology-oncology clinic once a week x 3 weeks for a total of four treatments (12 wks). Chemo is IV and infusion takes one to two hours. Follow-up in clinic is q 4 mo. X 2 yrs, q 6 mo. thereafter.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 3. The total number enrolled study-wide is 279, if multi-site study. Grade 4 toxicities include 1 WBC, 30 granulocytes/bands, 3 lymphocytes, 1 other hematologic, 1 vomiting, 1 diarrhea, 1 other GI, 1 alopecia, 2 dyspnea, 1 phlebitis/thrombosis, 1 malaise/fatigue, and 1 prothrombin time. Adverse event reported February 4, 2002.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

**TITLE:** CALGB 9741 - A Randomized Phase III Trial of Sequential Chemotherapy Using Doxorubicin, Paclitaxel and Cyclophosphamide or Current Doxorubicin and Cyclophosphamide Followed by Paclitaxel at 14 or 21 Day Intervals in Women with Node Positive Stage II/IIIA Breast Cancer

**KEYWORDS:** Chemotherapy, sequential, concurrent

**PRINCIPAL INVESTIGATOR:** COL Joseph Drabick, MC  
**ASSOCIATES:**

**DEPARTMENT:** Medicine  
**SERVICE:** Hematology-Oncology

**STATUS:** O  
**INITIAL APPROVAL DATE:** 16 December 1997

### STUDY OBJECTIVE

To compare sequential chemotherapy with doxorubicin, paclitaxel and cyclophosphamide to combined doxorubicin and cyclophosphamide followed by paclitaxel for disease-free survival and overall survival, and for toxicity. To determine whether increasing the dose density of adjuvant chemotherapy (decreasing the interval between chemotherapy from 21 to 14 days) will improve overall and disease-free survival.

### TECHNICAL APPROACH

Eligible patients will be randomly assigned to one of 4 groups. All will receive Adriamycin, Taxol and Cytosan (ATC). The 4 treatment plans are: 1) sequential C q3 weeks x 4, 2) sequential A-T-C q 2 weeks x 4, 3) concurrent AC q 3 weeks x 4 followed by T q 3 weeks x 4, 4) concurrent AC q2 weeks x 4 followed by T q 2 weeks x 4. Patients randomized to q 2-week therapy will receive G-CSF during therapy; the other groups receive G-CSF at the physician's discretion. Follow-up after treatment is q 6 months x 5 years, and yearly thereafter.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's last review there have been no publications reporting any data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 5. The total number enrolled study-wide is 2005, if multi-site study. Grade 4 toxicities include 1 platelet, 1 hemoglobin, 134 granulocytes/bands, 131 lymphocytes, 2 other hematologic, 3 nausea, 13 vomiting, 3 diarrhea, 1 stomatitis, 32 WBC, 5 dyspnea, 1 other pulmonary, 1 cardiac function, 1 ischemia, 1 embolism, 1 edema, 1 sensory, 1 cerebellar, 1 mood, 1 pain, 2 skin, 1 allergy, 1 fever w/o infection, 1 myalgias/arthritis, 2 hyperglycemia, 1 other endocrine, and 1 infection. This study closed effective March 31, 1999. Adverse events reports February 1, 2001, and April 24, 2001.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.



## DETAIL SUMMARY SHEET

TITLE: CALGB 9762 - Clinical Pharmacology of Paclitaxel in Relation to Patient Age

KEYWORDS: Pharmacology, paclitaxel, patient age

PRINCIPAL INVESTIGATOR: COL Joseph J. Drabick MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology Oncology

INITIAL APPROVAL DATE: 27 January 1998

### STUDY OBJECTIVE

To determine if there is a relationship between pharmacokinetic measurements of paclitaxel and aging. To determine if there is a relationship between the toxicities of paclitaxel and aging.

### TECHNICAL APPROACH

Eligible patients with cancer for whom single agent paclitaxel treatment is appropriate will receive standard paclitaxel treatment as described in protocol with protocol specific pharmacokinetic blood samples drawn prior to therapy and at 1, 6, and 7 hours after completion of first cycle of paclitaxel. All further treatment is at physician discretion. All patients will be followed in the out-patient oncology clinic for six weeks following protocol therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no new publications/literature reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 12. The total number enrolled study-wide is 158, if multi-site study. Grade 4 toxicities include 4 WBC, 20 granulocytes/bands, 24 lymphocytes, 1 infection, 1 vomiting, 1 cardiac function and 1 malaise/fatigue. Adverse events reported Nov 12, 1998, Nov 23, 1998, Dec 29, 1998, Aug 17, 1999, Jan 10, 2000, Mar 1, 2000, Oct 30, 2000 and Jan 12, 2001. We received a message that this study will permanently close to new patient accrual effective November 27, 2002.

Ref: CALGB Statistical Report 2002

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9781 - A Phase III Trial Comparing Trimodality Therapy (Cisplatin, 5-FU, Radiotherapy and Surgery) to Surgery Alone for Esophageal Cancer

KEYWORDS: esophageal, cancer, trimodality

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 24 February 1998

### STUDY OBJECTIVE

To compare overall 5-year survival rates between the two treatment arms. To compare treatment failure at 5 years between the two treatment arms. To assess and compare the toxicities of each approach.

### TECHNICAL APPROACH

Eligible patients with esophageal cancer will be randomized to receive either:

1. A combination of standard dose radiation therapy and chemotherapy with Cisplatin and 5-FU, given as outpatient therapy and lasting 5 1/2 weeks. This therapy is followed in 3 to 8 weeks with surgical esophageal resection requiring an 8 to 10 day hospital stay.
2. Standard treatment consisting of surgical esophageal resection requiring an 8 to 10 day hospital stay. All patients will be followed 4x per year for 2 years, 2x per year for an additional 2 years, then annually.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications since this protocol's last review.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 56, if multi-site study. Grade 4 toxicities include 2 WBC, 2 granulocytes/bands, 5 lymphocytes, 1 vomiting, 4 esophagitis/dysphagia, 2 anorexia, 1 cardiac function, and 1 phlebitis/thrombosis. Adverse events reported February 7, 2000 and July 18, 2002. This study was closed effective March 30, 2000.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

**TITLE:** CALGB 9730 - Single-Agent vs. Combination Chemotherapy in Advanced NSCLC - A CALGB Randomized Trial of Efficacy, Quality of Life and Cost-Effectiveness

**KEYWORDS:** NSCLC, advanced combination

**PRINCIPAL INVESTIGATOR:** Drabick, Joseph COL MC

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Hematology-Oncology

**INITIAL APPROVAL DATE:** 24 March 1998

### STUDY OBJECTIVE

To compare overall survival and quality of life of patients treated with paclitaxel alone or in combination with carboplatin. To determine cost-utility and cost-effectiveness of the best strategy. To compare response rates and toxicities of each arm.

### TECHNICAL APPROACH

Eligible patients will be randomized to receive IV chemotherapy treatment with either single-agent taxol or with a combination of taxol and carboplatin. This treatment will be on out-patient basis, requiring six six-hour visits over 18 weeks. Quality of life questionnaires will be administered at outset and at 2, 6, 9, and 12 months after registration to the study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been one publication reporting data on this study since last year's annual progress report.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 12. The total number enrolled study-wide is 584, if multi-site study. Grade 4 toxicities include 29 WBC, 3 platelets, 6 hemoglobin, 150 granulocytes/bands, 99 lymphocytes, 2 other hematologic, 2 hemorrhage, 6 infection, 2 nausea, 3 vomiting, 4 diarrhea, 1 esophagitis/dysphagia, 1 anorexia, 3 other GI, 2 bilirubin, 2 transaminase, 1 BUN, 3 alopecia, 5 dyspnea, 1 non-infect. pneumonia, 1 pleural effusion, 2 Ards, 4 other pulmonary, 7 dysrhythmia, 1 other heart, 1 hypotension, 1 phlebitis/thrombosis, 2 constipation, 3 pain, 3 allergy, 1 myalgias/arthralgias, 6 malaise/fatigue, 8 hyperglycemia, 1 hypocalcemia, 1 hyponatremia, 2 prothrombin time, and 3 other miscellaneous. Grade 5 toxicities include 1 hyperglycemia. Adverse events reported Jul 12, 99, Oct 13, 99, Nov 22, 99, Nov 15, 00, Jan 18, 01, Jan 22, 01, Mar 12, 01, Jan 14, 02, and Apr 4, 02. This study closed to enrollment December 29, 2000.

Ref: CALGB Statistical Report

### CONCLUSIONS

No conclusions have been reached.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9011 - A Study of Fludarabine vs. Chlorambucil vs. Both Drugs for Chronic Lymphocytic Leukemia

KEYWORDS: fludarabine, chlorambucil, crossover study

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 27 November 1990

### STUDY OBJECTIVE

To compare the response rates and progression-free survival in previously untreated chronic lymphatic leukemia (CLL) patients using three therapeutic regimens; to determine whether the quality-of-life is superior in any one of the regimens; to determine whether the two drugs fludarabine and chlorambucil are non-resistant by a crossover design for patients failing to respond to the initial single agent.

### TECHNICAL APPROACH

Randomized study for eligible CLL patients comparing the new drug fludarabine with the standard treatment of chlorambucil, or with the two drugs given in combination. Length of treatment depends on patient's response, with the maximum treatment being 2 years. Fludarabine is given intravenously for 5 days every 28 days. Chlorambucil is given by mouth for 1 day every 28 days. On 02 May 94, an addendum closed the third arm of the study. In September 1994, the consent form was revised to include new toxicity data and add new subjects.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been no publications reporting data from studies with similar design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 4. The total number enrolled study-wide is 544, if multi-site study. Grade 4 toxicities include 29 wbc, 35 platelets, 21 hemoglobin, 50 granulocytes/bands, 38 lymphocytes, 2 other hematologic, 2 hemorrhage, 5 infection, 2 vomiting, 1 diarrhea, 2 bilirubin, 2 transaminase (SGOT), 1 alk phos/5 nucleo, 1 creatinine, 1 proteinuria, 1 hematuria, 6 dyspnea, 1 ards, 1 other pulmonary, 2 dysrhythmia, 2 ischemia, 1 other heart, 1 hypotension, 1 edema, 1 cortical, 1 pain, 2 skin, 1 fever w/o infection, 2 malaise/fatigue, 1 hyperglycemia, 1 hypoglycemia, 1 hypercalcemia, 2 hyponatremia, and 1 partial thrombopla. Grade 5 toxicities include 1 platelets, 1 hemorrhage, 1 infection, 1 other heart, and 1 other neurologic. This study was closed to accrual effective December 9, 1994. Adverse events reported February 3, 1995, October 13, 1998, November 12, 1998, and July 19, 2002.

Ref: CALGB Statistical Report

### CONCLUSIONS

This study has identified fludarabine as a highly effective agent in the treatment of CLL. Other analysis continues.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9712 - A Randomized Phase II Study of Concurrent Fludarabine+Chimeric Anti-CD 20 Monoclonal Antibody IDEC-C2B8 (Rituximab) [NSC #6887451] Induction/Consolidation vs. Fludarabine Induction/Rituximab Consolidation

KEYWORDS: Fludarabine, Rituximab, Phase II

PRINCIPAL INVESTIGATOR: COL Joseph Drabick MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 28 April 1998

### STUDY OBJECTIVE

- 1) To determine in Fludarabine treated CLL patients the complete response (CR) rate and toxicity profile of concurrent and consolidative IDEC-C2138 (arm I) and of consolidative IDEC-C2D8 therapy (arm II).
- 2) To assess the CR rate in patients receiving concurrent therapy with IDEC-C2B8 and Fludarabine (the induction phase of arm I).

### TECHNICAL APPROACH

Eligible CLL patients will be randomly assigned to Arm I - Fludarabine plus Rituximab induction followed by Rituximab consolidation therapy, or to Arm II - Fludarabine induction (standard therapy) followed by Rituximab consolidation therapy. Induction therapy will last six months followed by a monitoring phase of twelve weeks. If appropriate, patients with CR, partial response, or stable disease will receive four weeks of consolidation therapy. Patients will receive prophylactic allopurinol for the first fifteen days of treatment. Patients will be entered on CALGB 9665-tissue bank companion study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

As reported in last years APR there have been no publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 11. The total number enrolled study-wide is 104, if multi-site study. Grade 4 toxicities include 8 WBC, 3 platelets, 1 hemoglobin, 16 granulocytes/bands, 22 lymphocytes, 1 bilirubin, 2 dyspnea, 1 PO2/PCO2, and 1 hyperglycemia. Adverse events reported April 22, 1999, July 8, 1999, July 20, 1999, August 19, 1999, June 15, 2000, and June 4, 2002. This study was closed to accrual effective January 31, 2000.

Ref: CALGB Statistical Report

### CONCLUSIONS

Study analysis is ongoing.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9732 - A Randomized Phase III Study Comparing Etoposide and Cisplatin with Etoposide, Cisplatin and Paclitaxel in Patients with Extensive Small Cell Lung Cancer

KEYWORDS: phase III, small cell lung cancer, extensive

PRINCIPAL INVESTIGATOR: Joseph Drabick, COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: C  
INITIAL APPROVAL DATE: 28 July 1998

### STUDY OBJECTIVE:

To determine whether the addition of paclitaxel to standard chemotherapy treatment (etoposide/cisplatin) improves the survival of patients with extensive SCLC.

To compare tumor response rate and failure-free survival of patients in these two treatments groups.

To describe and compare the toxicities of patients in these two treatment groups.

### TECHNICAL APPROACH

Eligible patients with extensive SCLC will be randomized to 1) standard chemotherapy: etoposide/cisplatin IV as 3 day treatment q 21 days for a total of 6 treatments, or to 2) standard chemotherapy as above with IV paclitaxel in addition on day one of each treatment. Treatment will be in Hematology-Oncology clinic.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been one abstract reporting data on this study since last APR.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1 (now deceased). The total number enrolled study-wide is 587, if multi-site study. Grade 4 toxicities include 78 WBC, 33 platelets, 5 hemoglobin, 174 granulocytes/bands, 63 lymphocytes, 3 other hematologic, 4 nausea, 20 vomiting, 8 diarrhea, 1 stomatitis, 6 anorexia, 2 other GI, 1 bilirubin, 1 other liver, 5 creatinine, 7 other kidney/bladder, 7 dyspnea, 8 other pulmonary, 5 dysrhythmia, 1 ischemia, 6 other heart, 1 motor, 5 other neurologic, 1 allergy, 13 fever w/o infection, 1 myalgias/artralgias, 3 other flu-like symptoms, and 33 other miscellaneous. Grade 5 toxicities include 5 WBC, 2 other hematologic, 1 vomiting, 2 other hematologic, 1 vomiting, 2 other kidney/bladder, 2 dyspnea, 3 other pulmonary, 1 dysrhythmia, 1 ischemia, 1 other heart, 1 other neurologic, 1 fever w/o infection, 1 other flu-like symptoms, and 18 other miscellaneous. Adverse event reported Dec 5, 2000. This study was closed to accrual effective July 31, 2001. WRAMC is closing this study. The only patient enrolled is now deceased.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

**TITLE:** CALGB 39801- Concurrent Carboplatin, Paclitaxel, and Radiation Therapy Verses Induction Carboplatin and Paclitaxel Followed by Concurrent Carboplatin, Paclitaxel, and Radiation Therapy for Patients with Unresectable Non Small Cell Lung Cancer – A Phase III Trial

**KEYWORDS:** non small cell lung cancer, unresectable, chemoradiotherapy

**PRINCIPAL INVESTIGATOR:** Drabick, Joseph J. LTC MC  
**ASSOCIATES:**

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Hematology-Oncology

**INITIAL APPROVAL DATE:** 27 October 1998

**New Anniversary Month:** September

### STUDY OBJECTIVE

To determine whether the addition of two cycles of induction chemotherapy with carboplatin and Paclitaxel to concomitant chemoradiotherapy utilizing carboplatin and Paclitaxel leads to an increase in overall response rate, failure-free survival, and survival. To assess the pattern of failure on both treatment arms (loco-regional vs. distant failure). To assess the toxicity on both treatment arms.

### TECHNICAL APPROACH

All eligible patients will be randomized to one of two treatments: 1) Chemotherapy with Paclitaxel and carboplatin once a week combined with radiation therapy to the chest 5 days per week for a total of 7 weeks, or 2) chemotherapy with Paclitaxel and carboplatin, once every 3 weeks for 6 weeks followed by carboplatin and Paclitaxel once per week combined with radiation therapy to the chest 5 days per week for 7 weeks. Update #1, 3/15/99, containing editorial changes was submitted to DCI 4/21/99.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 366, if multi-site study. Grade 4 toxicities include 1 allergic reaction/hypersensitivity, 41 neutrophils/granulocytes (ANC), 15 leukocytes (total WBC), 22 lymphopenia, 1 transfusion: platelets, 1 supraventricular arrhythmias, 1 hypotension, 2 pericardial effusion/pericarditis, 1 cardiac-ischemia/infarction, 3 thrombosis/embolism, 1 cardiac troponinT (cTnT), 7 fatigue (lethargy/malaise), 1 alopecia, 1 radiation dermatitis, 13 anorexia, 10 dysphagia-esophageal related, 1 hemorrhage-other, 1 hemorrhage/bleeding with grade, 2 febrile neutropenia, 1 infection/other, 1 hyponatremia, 1 hypokalemia, 1 depressed level of consciousness, 1 pleuritic pain, 1 arthralgia (joint pain), 1 pain-other, a dyspnea (shortness of breath), 1 hiccoughs (hiccups/singultus), 1 pulmonary fibrosis, 5 pneumonitis/pulmonary infiltration, 1 adult respiratory distress syn, 1 hypoxia, and 1 pneumothorax. Grade 5 toxicities include 1 hemorrhage-other, 1 pneumonitis/pulmonary infiltration, and 1 pulmonary-other. This study closed to enrollment effective May 31, 2002.

**Ref:** CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 19805 - A Phase II Study of Flavopiridol (NSC # 649890) in Patients With Fludarabine Refractory B-Cell Chronic Lymphocytic Leukemia

KEYWORDS: Chronic Leukemia, refractory, investigational

PRINCIPAL INVESTIGATOR: Joseph Drabick, COL MC  
ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology Oncology Service

INITIAL APPROVAL DATE: 24 November 1998

### STUDY OBJECTIVE

To determine the complete response rate, partial response rate, and toxicity profile to flavopiridol therapy in patients with fludarabine refractory Chronic Lymphocytic Leukemia. To determine the effects of flavopiridol on normal t-cell subsets and immunoglobulin levels in these patients.

### TECHNICAL APPROACH

All eligible patients will receive flavopiridol by a continuous intravenous infusion for three days, repeated every two weeks for a maximum of 12 cycles (approximately six months). The first cycle will be given in the hospital and subsequent cycles as an out-patient utilizing an ambulatory infusion pump. Disease reevaluation will be done at the end of 4 and 8 cycles, as well as at completion of therapy. Blood and bone marrow samples will be collected prior to any therapy and submitted to CALGB Leukemia Tissue Bank.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications or literature reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 7. The total number enrolled study-wide is 53, if multi-site study. Grade 4 toxicities include 7 neutrophils/granulocytes (ANC), 1 hemoglobin, 3 platelets, and 1 diarrhea. Adverse events reported December 27, 2000, January 9, 2001, January 10, 2001, February 20, 2001, March 12, 2001, April 23, 2001, and August 9, 2001. This study has met its accrual goal and is now closed effective July 3, 2002.

Ref: Jun 02 CALGB Statistical Report

### CONCLUSIONS

Too early.



## DETAIL SUMMARY SHEET

TITLE: CALGB 8364 – Immunological Diagnostic Studies in Adult ALL

KEYWORDS: immunology, lymphocyte, leukemia

PRINCIPAL INVESTIGATOR: Joseph P. Drabick COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 25 October 1983  
New Anniversary Month: September

### STUDY OBJECTIVE

To determine the incidence of various monoclonal antibodies' cytochemical and conventional lymphoid markers in adult acute lymphatic leukemia (ALL). To correlate the presence of the various markers with the initial and subsequent clinical characteristics of the disease, response rate, and response duration. To determine if marker status changes at relapse.

### TECHNICAL APPROACH

Non-randomized study in which all eligible patients being entered on the ALL treatment protocol agree to allow, prior to the initiation of therapy, the submission of six air-dried unstained BM smears for confirmatory cytochemical studies and 2 cc of bone marrow aspirate, along with 7 cc of peripheral blood to a designated CALGB reference laboratory. The same set of samples is again obtained at relapse.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have not been any new publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 34. The total number enrolled study-wide is 953, if multi-site study. No grade 4 toxicities. This study closed to enrollment effective April 15, 1999.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early. Interim analysis continues on the value of immunophenotype in ALL.

## DETAIL SUMMARY SHEET

TITLE: CALGB 19801 - A Phase II Study of 506U78 in Patients With Refractory or Relapsed T-lineage Acute Lymphoblastic Leukemia (ALL) or Lymphoblastic Lymphoma (LBL)

KEYWORDS: refractory disease, investigational therapy, leukemia/lymphoma

PRINCIPAL INVESTIGATOR: Joseph Drabick, COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology Oncology

STATUS: C  
INITIAL APPROVAL DATE: 24 November 1998

### STUDY OBJECTIVE

To determine the complete and partial remission rates, as well as the remission duration, in patients with refractory or relapsed T-lineage acute lymphoblastic leukemia or lymphoblastic lymphoma receiving 506U78 (1.5 gram/m<sup>2</sup>/day) on an alternate day schedule (days 1,3,5). To determine the safety and toxicity associated with 506U78 administered on this schedule.

### TECHNICAL APPROACH

All eligible patients will receive the investigational drug, 506U78, intravenously over 2 hours on Days 1,3,5. Their disease will be reevaluated after 21 days. If not in remission, an identical course of treatment will be given. When remission occurs, consolidation therapy will be given. Two additional courses of the same therapy will be given as consolidation. Patients who achieve a complete response would then be candidates to receive a stem cell transplant. Those patients would be removed from this study, at that time, for transplant.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There were no publications reporting any data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 40, if multi-site study. Grade 4 toxicities include 11 neutrophils/granulocytes, 1 leukocytes (total wbc), 2 hemoglobin, 1 lymphopenia, 6 platelets, 1 fatigue (lethargy/malaise), 1 infection without neutropenia, and 1 depressed level of consciousness. Adverse events reported February 13, 2002. This study has met its' accrual goal and is closed effective September 12, 2001. This study can be closed here at Walter Reed because the one patient enrolled is now deceased.

Ref: Jun 02 CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 119801 - Telephone Monitoring: Early Identification of Psychological Distress In Cancer Patients 65 or More Years Old During Active Treatment

KEYWORDS: Advanced Cancer, psychosocial, telephone interview

PRINCIPAL INVESTIGATOR: Joseph Drabick, COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology Oncology

STATUS: O  
INITIAL APPROVAL DATE: 24 November 1998

### STUDY OBJECTIVE

To test whether telephone monitoring plus educational materials can reduce elderly cancer patient's psychological distress significantly more than the receipt of educational materials alone, through early identification of psychological problem and referral to treatment. To develop psychosocial profiles of older patients with advanced cancer who show the highest and lowest levels of psychological distress in, terms: of medical, psychosocial, and sociodemographic characteristics.

### TECHNICAL APPROACH

All eligible patients will be randomized to one of two groups. 1) Educational Materials Group: This group will be given educational materials that provide information about emotional problems which cancer patients may have and various agencies or services that are available to them. They will also be contacted by phone, by a trained psycho-oncology interviewer, three times during one year to discuss emotional and social issues. 2) Telephone Monitoring Group: This group, in addition to the educational materials, will receive a phone call from the psycho-oncology interviewer once a month for six months. The calls will last approximately 15 minutes each. Questions will ask about mood, social life issues, and physical problems. If problems are identified, follow up will be done by WRAMC Oncology nurse, physician, social service, or psychologist, depending upon the needs. A written questionnaire will be sent prior to the phone call describing the questions that will be asked.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 6 and the total enrolled to date at WRAMC is 17. The total number enrolled study-wide is 188, if multi-site study. This is a telephone survey. This study has a partial closure effective 15 January 2002 to enrolling patients with prostate cancer. It is still open to breast and/or colon cancer patients. Adverse event reported 28 November 2001.

Ref: June 2002 CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9865 - Tumor Replication Error (RER) Status and Outcome In A Colon Cancer Adjuvant Chemotherapy Trial

KEYWORDS: Tissue block, Dukes C Stage, Mutations

PRINCIPAL INVESTIGATOR: COL Joseph Drabick, MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 15 December 1998

### STUDY OBJECTIVE

To determine the relationship between disease free survival, overall survival, and tumor replication error (RER) status for individuals who have received adjuvant chemotherapy for colon cancer. To develop a database to study the relationship between family history, tumor RER status, and treatment outcome for individuals who have received adjuvant chemotherapy for colon cancer.

### TECHNICAL APPROACH

Phase I – All patients who were enrolled on CALGB 8896 for Dukes C Colon Cancer who have tissue blocks available will have two tissue blocks submitted for RER analysis (one with tumor, one with normal tissue). This will include patients who are deceased. The CALGB Pathology Coordinating office will submit a list to the institution of potentially eligible cases for Phase II. This phase involves obtaining consent for completion of a family questionnaire. For deceased patients, a chart review may be obtained and data collected to correlate treatment outcome, disease relapse and survival. The institution or the patient will not receive the results of the RER analysis.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been additional abstracts submitted reporting data.

The number of subjects enrolled to the study since last APR at WRAMC is 3 and the total enrolled to date at WRAMC is 5. The total number enrolled study-wide is 227, if multi-site study. This study closed to accrual effective 30 August 2002.

Ref: June 2002 CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9192 - Comparison of Chemotherapy vs. Chemohormonotherapy in Premenopausal Women with Stage II Receptor-Positive Breast Cancer

KEYWORDS: breast cancer, node-positive, receptor-positive

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 26 March 1991

### STUDY OBJECTIVE

To compare the recurrence rates, disease-free intervals and hormone receptor-positive survival for premenopausal women with lymph node-positive breast cancer given adjuvant therapy with cytoxan, Adriamycin, and 5-fluorouracil (CAF) chemotherapy alone, or chemotherapy followed by Zoladex, or chemotherapy followed by Zoladex and tamoxifen. To compare the relative toxicities of these three regimens and to assess their effect on blood hormone levels.

### TECHNICAL APPROACH

All eligible patients will receive a 6-month course (six cycles) of standard CAF therapy. Initially, they will be randomized to receive an additional 5 years of Zoladex, receive an additional 5 years of Zoladex and tamoxifen, or end therapy following CAF.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been a publication reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 13. The total number enrolled study-wide is 1330, if multi-site study. Grade 4 toxicities include 23 leukopenia, 55 granulocytes/bands, 1 lymphocytes, 1 thrombocytopenia, 1 anemia, 1 hemorrhage, 1 infection, 1 nausea, 2 vomiting, 1 diarrhea, 1 stomatitis, 1 liver, 1 cardiac, 1 phlebitis, 1 local, 1 neuro-motor, 2 neuro-psych, 1 neuro-clinical, 1 metabolic, 1 coagulation, 2 diabetes, and 1 others. Grade 5 toxicities include 1 infection, 1 pulmonary, 2 cardiac, and 1 neuro-psych. Adverse events reported Sept 5, 96, Jul 11, 97, Jun 1, 98, Nov 30 99, and May 30, 02. This study closed to accrual effective February 1, 1994.

Ref: CALGB Statistical Report

### CONCLUSIONS

Analysis is ongoing. No conclusions have been reached.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9840 - A Phase III Study of Paclitaxel Via Weekly 1 Hour Infusion Versus Standard 3 Hour Infusion Every 3 Weeks with Herceptin (Trastuzumab) (NSC #688097) in the Treatment of Patients with/without HER-2/NEU-Overexpressing Metastatic Breast Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL, MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 15 December 1998

### STUDY OBJECTIVE

To determine if "dose dense" treatment with paclitaxel via weekly 1-hour infusion significantly improves the response rate as compared to "standard" paclitaxel treatment for metastatic breast cancer. To evaluate the time to progression and survival of patients with metastatic breast cancer treated with either "dose dense" or "standard" paclitaxel.

### TECHNICAL APPROACH

Patients will be randomized to receive either paclitaxel, 175mg/m<sup>2</sup> over 3 hours every 3 weeks or to paclitaxel 100mg/m<sup>2</sup> over 1 hour every week for the first 6 weeks with subsequent infusions of paclitaxel at 80mg/m<sup>2</sup> over 1 hour. Both regimens will be given until development of progressive disease, major toxicity, or patient withdraws consent. Follow-up will be done until progression, initiation of non-protocol therapy, or death, whichever occurs first.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this study or from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 2 and the total enrolled to date at WRAMC is 7. The total number enrolled study-wide is 433, if multi-site study. Grade 4 toxicities include 6 WBC, 1 platelet, 19 granulocytes/bands, 21 lymphocytes, 3 infection, 2 anorexia, 2 other GI, 1 bilirubin, 6 dyspnea, 1 PO<sub>2</sub>/PCO<sub>2</sub>, 1 pulmonary edema, 2 ARDS, 2 other pulmonary, 1 dysrhythmia, 1 hypotension, 1 phlebitis/thrombosis, 1 edema, 1 vision, 1 allergy, 1 malaise/fatigue, 4 hyperglycemia, 1 hypocalcemia, 1 hyponatremia, 1 hypokalemia, and 1 other miscellaneous. Adverse events reported March 13, 2001, and September 19, 2001.

Ref: June 2002 CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9194 - Comparison of Adjuvant chemotherapy with Concurrent or Delayed Tamoxifen vs. Tamoxifen Alone in Postmenopausal Patients with Receptor Positive Stage II Breast Cancer

KEYWORDS: postmenopausal, lymph node positive, receptor positive

PRINCIPAL INVESTIGATOR: COL Joseph Drabick MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 30 April 1991

### STUDY OBJECTIVE

To compare disease-free survival and overall survival of postmenopausal primary breast cancer patients with involved axillary nodes and positive estrogen and/or progesterone receptors treated with standard adjuvant therapy with long-term tamoxifen, or with chemo endocrine therapy with combined cytoxan, Adriamycin, and 5-fluorouracil (CAF) followed by long-term tamoxifen, or with concurrent chemo endocrine therapy with tamoxifen and CAF.

### TECHNICAL APPROACH

For 5 years, six courses of CAF followed by tamoxifen for 5 years, or six courses of CAF with concurrent tamoxifen for 5 years. Four addenda to this study were sent to the IRB and approved in the past year.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 3. The total number enrolled study-wide is 1539, if multi-site study. Grade 4 toxicities include 1 abdominal pain, 4 anemia, 1 cardiac -EF/CHF, 3 diarrhea, 403 granulocytopenia, 1 infection, 229 leukopenia, 1 local, 1 lymphopenia, 4 phlebitis/thrombosis/embolism, 1 prothrombin time increase, 7 stomatitis, 14 thrombocytopenia, and 1 vomiting. Grade 5 toxicities include 1 infection, 1 metabolic-other, and 1 phlebitis/thrombosis/embolism. Adverse event reported Sept 15, 1997. Study closed to accrual effective July 15, 1995.

Ref: CALGB Statistical Report

### CONCLUSIONS

Analysis is ongoing.

## DETAIL SUMMARY SHEET

TITLE: CALGB 8461 - Cytogenic Studies in Acute Leukemia - A Companion Study to CALGB 8011, 8323, 8321, and 8411

KEYWORDS: cytogenics, acute leukemia

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 25 September 1984

### STUDY OBJECTIVE

To determine the incidence of specific chromosome abnormalities in adult acute non-lymphatic leukemia (ANLL) and acute lymphatic leukemia (ALL).

### TECHNICAL APPROACH

All eligible patients are registered to this companion to treatment protocols. A specimen of marrow and blood is obtained at diagnosis and again at relapse.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no additional publications added but there were prior publications now listed.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 104. The total number enrolled study-wide is 5025, if multi-site study. No toxicities reported.

Ref: CALGB Statistical Report July 2003

### CONCLUSIONS

Too early.



## DETAIL SUMMARY SHEET

TITLE: CALGB 9111 – A Trial of G-CSF vs. Placebo During Remission Induction and Consolidation Chemotherapy for Adult Acute Lymphatic Leukemia

KEYWORDS: adult acute leukemia, G-CSF

PRINCIPAL INVESTIGATOR: Joseph P. Drabick COL MC

DEPARTMENT: Medicine

SERVICE: Hematology-Oncology

STATUS: O

INITIAL APPROVAL DATE: 25 October 1991

New Anniversary Month: September

### STUDY OBJECTIVE

To: 1) compare time to bone marrow recovery, infection incidence, days of hospitalization, and tolerance of non-hematopoietic organs after intensive chemotherapy for acute lymphatic leukemia (ALL) in patients given either granulocytes colony-stimulating factor (G-CSF) or placebo; 2) determine G-CSF's effect on CR rate and duration and mortality (during neutropenia) during intensive induction and intensification; and 3) compare doses that can be given to G-CFS vs. placebo patients.

### TECHNICAL APPROACH

Eligible patients will be randomly assigned to receive subcutaneous injections of either G-CSF or placebo starting 3 days after initial chemotherapy. Injections will continue until the white blood count is normal. The pharmacist will be the only one who knows what the patients will be receiving. The study will remain blinded until after the first month. After being unblinded, patients who received G-CSF will continue to receive it during the next course of therapy. Those who did not will not receive any further placebo or G-CSF. Patients will receive a series of five different cancer treatments in sequence; each uses combination chemotherapy, and one involves radiation. Total treatment time is 24 months.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been a couple of publications reporting data since last APR.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 8. The total number enrolled study-wide is 198, if multi-site study. There was an adverse event reported July 7, 1993 and September 16, 1996. Grade 4 toxicities include 238 WBC, 199 platelets, 57 Hgb, 231 grans/bands, 174 lymphocytes, 3 hemorrhage, 12 infection, 37 bilirubin, 3 transaminase, 2 Alk Phos, 1 liver, 1 creatinine, 2 renal, 7 hypotension, 1 amylase, 7 hyperglycemia, 8 hypocalcemia, and 12 fibrinogen. Grade 5 toxicities include 1 hemorrhage, 3 infections, 1 renal, and 1 hypotension. This study was closed effective July 30, 1993 – met accrual goal and CALGB 9311 would soon be open.

Ref: CALGB Statistical Report

### CONCLUSIONS

This study has shown that treatment with G-CSF is effective during induction chemotherapy for ALL. Other results are still undergoing analysis.

## DETAIL SUMMARY SHEET

TITLE: CALG13 9862 - Molecular Genetic Features of Acute Lymphoblastic Leukemia

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 22 June 1999

### STUDY OBJECTIVE

To use PCR analysis to identify patients with p190 and p210 BCR-ABL positive ALL and to evaluate the clinical significance of these fusion transcripts measured at time of diagnosis. To evaluate the clinical significance of MDR as defined by BCR-ABL fusion transcripts in patients who have achieved a complete response, using both qualitative RT-PCR and quantitative (Real Time) PCR in sequential samples of both blood and bone marrow. To compare blood with bone marrow samples for the detection and quantitation of BCR-ABL transcripts in diagnosis and sequential remission samples. To pilot PCR detection and quantitation of WT-1 expression at diagnosis, remission, and at relapse in BCR-ABL positive and negative ALL, and to determine the impact of this marker on clinical outcome.

### TECHNICAL APPROACH

All patients enrolled on the CALGB Leukemia treatment study (currently 19802) will be offered participation in this companion study. A total of 8 plus samples of blood and bone marrow will be collected and sent to the CALG13 Leukemia Tissue Bank in Columbus, Ohio. The number of samples is dependent upon response to therapy and if the disease returns after remission. The tests will only be drawn at a time when diagnostic blood and bone marrow samples would ordinarily be taken.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been a couple of publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 108, if multi-site study. No toxicities reported. No adverse events reported.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

**TITLE:** CALGB 19802 Phase II Study in Adults with Untreated Lymphoblastic Leukemia Testing Increased Doses of Daunorubicin During Induction, and Cytarabine During Consolidation, Followed by High-Dose Methotrexate and Intrathecal Methotrexate in Place of Cranial Irradiation

**KEYWORDS:** ALL, Dose escalation, High-dose methotrexate

**PRINCIPAL INVESTIGATOR:** Joseph Drabick, COL MC

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Hematology-Oncology

**INITIAL APPROVAL DATE:** 31 August 1999

**NEW ANNIVERSARY DATE:** 31 July

**STUDY OBJECTIVE:** To evaluate the complete response (CR) rate and toxicity in patients < 60 years of age when three days of daunorubicin are given at 60mg/m<sup>2</sup>/day in Module A and then, if tolerated, when doses of daunorubicin are escalated to 80 mg/m<sup>2</sup>/day. To evaluate CR rate and toxicity in patients > 60 years of age when three days of daunorubicin are given at 60 mg/m<sup>2</sup>/day during Module A without cyclophosphamide. To evaluate the toxicity of three days of cytarabine at 2000 mg/m<sup>2</sup>/day IV over three hours during post-remission therapy (Module B). To measure the CNS relapse rate of ALL when prophylactic intrathecal and high dose intravenous chemotherapy (Module C) replaces cranial irradiation. To target a specific serum methotrexate level at 30 hours following initiation of IV methotrexate infusion.

**TECHNICAL APPROACH:** All eligible patients who continue to show a response to therapy will receive a seven-course regimen of various chemotherapy agents. Doses of daunorubicin will be different for patients under 60 years than for patients over 60 years. During Course three, high doses of methotrexate will be given in place of standard cranial irradiation for CNS prophylaxis. Serum levels will be monitored to ensure adequate dosing. The seven-course therapy will take 24 months to complete. Post therapy monitoring will be done every 3-6 months for three years after treatment, then annually. Two additional companion studies are required for participation. These studies have separate consent forms but do require submission of blood and bone marrow samples for correlative science with response of the disease to therapy.

**PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE** Since this protocol's review last years, there have been a couple abstracts published. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 163, if multi-site study.

This study closed on January 5, 2001 after meeting its accrual goals. Grade 4 toxicities include 123 neutrophils/granulocytes, 21 leukocytes, 1 hemolysis, 23 hemoglobin, 6 lymphopenia, 108 platelets, 3 transfusions: platelets, 1 transfusion: pRBCs, 1 ventricular arrhythmia, 1 cardiac left ventricular func., 6 hypotension, 4 edema, 1 DIC, 3 fibrinogen for leukemia, 2 fatigue, 1 endocrine-other, 8 anorexia, 3 dysphagia/esophagitis/odyn, 1 stomatitis/pharyngitis, 1 pancreatitis, 1 constipation, 1 vomiting, 1 CNS hemorrhage/bleeding, 2 hemorrhage/bleeding with grade, 1 liver dysfunction/failure, 1 SGOT(AST), 2 SGPT (ALT), 6 bilirubin, 1 infection without neutropenia, 1 catheter-related infection, 2 febrile neutropenia, 16 infection, 5 hypocalcemia, 1 hyponatremia, 2 hyperkalemia, 1 hypokalemia, 2 hypermagnesemia, 4 acidosis, 1 alkalosis, 1 bicarbonate, 4 hyperglycemia, 1 arachnoiditis/meningismus/radi, 1 leukoencephalopathy associated, 1 pyramidal tract dysfunction, 2 speech impairment, 1 depressed level of consciousness, 2 ataxia, 1 confusion, 1 neuropathy-sensory, 1 neuropathy cranial, 6 dyspnea, 2 pleural effusion, 1 pneumonitis/pulmonary infilt., 3 adult respiratory distress syn., 4 hypoxia, 2 creatinine, and 5 renal failure. Grade 5 toxicities include 1 CNS hemorrhage/bleeding, 1 hemorrhage/bleeding with grade, 1 febrile neutropenia, 8 infection, 1 neurologic-other, and 4 pulmonary-other. Ref: CALGB Statistical Report. One adverse event reported for this study (November 21, 2001).

**CONCLUSIONS** Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9190: A Trial of Postoperative Interferon in Resected High Risk Melanoma

KEYWORDS: high-dose interferon, low-dose interferon, observation

PRINCIPAL INVESTIGATOR: COL Joseph J. Drabick MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology Oncology

INITIAL APPROVAL DATE: 2 January 1992

### STUDY OBJECTIVE

To establish the efficacy of interferon alfa-2b as an adjuvant in increasing the disease-free survival and overall survival in patients at high risk for recurrence after definitive surgery for deep primary lesions or after regional lymph node recurrence

### TECHNICAL APPROACH

Eligible patients are randomized to receive one of three treatment plans: (1) high-dose interferon for approximately 1 year; (2) low-dose interferon for approximately 2 years; or (3) observation-only frequent follow-up for 2 years, then annually. Those patients randomized to receive interferon will be trained to self-administer their subcutaneous injections at home.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been no publications reporting data on this or other studies with similar study design.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 642, if multi-site study. Grade 4 toxicities include 7 granulocytopenia, 1 vomiting, 2 diarrhea, 1 dehydration, 1 liver, 1 cardiac, 1 neurologic (motor), 2 neurologic (psycho), 2 fatigue, 1 metabolic, 1 hyperlipidemia, 5 myalgias, 1 arthralgia, and 1 anemia. Grade 5 toxicities include 1 hemorrhage, and 1 cardiac. No adverse events reported. This study was closed to accrual June 1, 1995.

Ref: CALGB Statistical Report

### CONCLUSIONS

No conclusion as of yet.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9195 - A Trial of Adjuvant Chemoradiation vs. Observation After Gastric Resection of Adenocarcinoma

KEYWORDS: post-gastrectomy, adjuvant therapy, observation

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC

ASSOCIATES:

DEPARTMENT: Medicine

SERVICE: Hematology Oncology

STATUS: O

INITIAL APPROVAL DATE: 2 January 1992

### STUDY OBJECTIVE

To compare overall and disease-free survival between patients treated with gastrectomy only, and those treated with gastrectomy plus adjuvant therapy; to compare the incidence and patterns of disease failure between these two groups of patients; and to assess patient tolerance of upper abdominal chemoradiation after gastric resection.

### TECHNICAL APPROACH

Eligible patients will be randomized to receive either adjuvant chemoradiation, consisting of five courses of 5-fluorouracil and leucovorin plus one course of radiation, or to observation only. This arm would consist of close observation for symptoms of recurrence over a 2-year period, then annual follow-up thereafter.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications since this protocol's last review.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 603, if multi-site study. Grade 4 toxicities include 1 alk phos or 5' nucleo inc, 1 cardiac-dysrhythmia, 1 circulatory (other), 1 creatinine increase, 8 diarrhea, 1 dyspnea, 67 granulocytopenia, 1 hyperglycemia, 1 hypertension, 1 hypotension, 1 ileus, 1 infection, 13 leukopenia, 1 lymphopenia, 1 somnolence/agitation, 5 stomatitis, 1 thrombocytopenia, 6 vomiting, and 1 wound infection. Grade 5 toxicities include 1 infection and 1 lung (other). No adverse events reported. This study was closed effective July 15, 1998.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9191 - A Randomized Study of All-Trans Retinoic Acid vs. Standard Induction Therapy for Acute Promyelocytic Leukemia

KEYWORDS: induction, consolidation, crossover

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 24 November 1992

### STUDY OBJECTIVE

To compare the complete remission rate and disease-free survival of trans retinoic acid (TRA) to that achieved with conventional induction chemotherapy, including Cytosine Arabinoside plus daunorubicin, in patients with previously untreated acute promyelocytic leukemia; to compare the toxicities of TRA to those of cytosine/daunorubicin as induction therapy; and to determine the value of maintenance therapy with TRA.

### TECHNICAL APPROACH

All eligible patients will be initially randomized to receive one of two induction treatments: 1) TRA orally for 45-90 days; or 2) standard chemotherapy with cytosine and daunorubicin for 7 days total. Once a complete response is achieved, consolidation therapy will be given for two courses with cytosine, one course being high dose. If the response remains, the patient is randomized again to receive either maintenance therapy with TRA or observation alone. If the leukemia returns after a response is achieved and the patient was randomized to TRA, they will crossover to receive the second therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are some publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 401, if multi-site study. Grade 4 toxicities include 164 WBC, 196 platelets, 11 hemorrhage, 14 infection, 1 vomiting, 5 stomatitis, 25 liver-clinical, 20 pulmonary, 5 cardiac, 1 motor, 3 skin, 4 metabolic, 2 coagulation, 1 pulmonary embolus, and 1 diarrhea. Grade 5 toxicities include 20 hemorrhage, 10 infection, 1 liver-clinical, 4 pulmonary, and 2 cardiac. Adverse event reported September 28, 2001. This study was closed to accrual effective Feb 1, 1995.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9222 - A Randomized Study of Intensification Therapy for Patients under Age 60 with Acute Myelogenous Leukemia

KEYWORDS: post-remission, high-dose cytosine, sequential therapy

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 24 November 1992

### STUDY OBJECTIVE

To compare two post-remission chemotherapy regimens: 1) intensification with single-agent high-dose cytosine arabinoside; and 2) three courses of sequential, potentially non-cross-resistant treatment. To confirm patient tolerance, and to continue to investigate the prognostic significance of cytogenetics and immunophenotyping in-patients with acute myelogenous leukemia.

### TECHNICAL APPROACH

All eligible patients will receive the same standard induction -- up to two times if necessary -- to achieve a complete response. Responders will then be randomized to receive either 1) six high doses of cytosine arabinoside repeated at 28-day intervals for a total of three courses, or 2) six sequential doses of high dose cytosine, followed by a second cycle of cyclophosphamide and etoposide, and then a third cycle of diaziquone and mitoxantrone with granulocyte colony-stimulating factor. Patients will then be followed for relapse or survival.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 5. The total number enrolled study-wide is 474, if multi-site study. Grade 4 toxicities include 348 WBC, 348 platelets, 75 hemoglobin, 346 granulocytes/bands, 303 lymphocytes, 4 other hematologic, 8 hemorrhage, 53 infections, 1 nausea, 6 vomiting, 15 diarrhea, 11 stomatitis, 8 esophagitis/dysphag, 14 anorexia, 3 other GI, 55 bilirubin, 1 other mucosal, 12 transaminase (SGOT), 2 alk phos/5' nucleot, 2 liver-clinical, 1 other liver, 5 creatinine, 5 hematuria, 13 renal failure, 2 other kidney/bladder, 38 dyspnea, 14 O2/PCO2, 12 pulmonary edema, 4 non-inf. Pneumonia, 16 ARDS, 11 other pulmonary, 20 dysrhythmia, 4 cardiac function, 4 ischemia, 4 pericardial, 4 other heart, 2 hypertension, 24 hypotension, 2 skin, 8 fever w/o infection, 20 malaise/fatigue, 15 hyperglycemia, 2 hypoglycemia, 15 hypocalcemia, 5 hypomagnesemia, 3 hyponatremia, 6 hypokalemia, 1 other metabolic, 7 prothrombin time, 5 partial thromboplas, and 1 eye. Grade 5 toxicities include 1 platelets, 7 infections, 3 ARDS, 1 other pulmonary, 1 cardiac function, and 1 cerebellar. Adverse events reported 1 December 1994, 20 June 1996, 10 October 1996, and 24 February 1997. This study was closed to accrual 31 December 1995.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9153 - A Trial of Cladribine in Advanced Stage, Low-Grade Non-Hodgkin's Lymphoma

KEYWORDS: low-grade, lymphoma, advanced

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 30 March 1993

### STUDY OBJECTIVE

To: 1) determine the percentage of patients with advanced, previously untreated, low-grade lymphomas who respond with complete or partial remissions to treatment with Cladribine, 2) estimate the duration of response for patients with partial and complete responses, and 3) describe the toxicity of Cladribine treatment in this population.

### TECHNICAL APPROACH

All eligible patients will be registered and will receive treatment with Cladribine intravenously as a 2-hour infusion for 5 consecutive days, every 28 days. A maximum of six cycles will be given. All patients will be reevaluated every two cycles for response.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been no publications reporting data from studies with similar study design in the literature. The objectives of this investigation have not been fulfilled by prior studies.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 44, if multi-site study. Grade 4 toxicities include 7 WBC, 1 hemoglobin, 13 granulocytes/bands, 19 lymphocytes, 1 hemorrhage, and 1 infection. No adverse events reported. This study closed to accrual effective December 15, 1993.

Ref: CALGB Statistical Report

### CONCLUSIONS

Analysis showed this therapy to have a level of antineoplastic activity. No conclusion has been reached.



## DETAIL SUMMARY SHEET

TITLE: CALGB 9082 - Trial Study of High-Dose CPA/CDDP/BCNU and ABMS as Consolidation to Adjuvant CAF for Patients With Operable Stage II or Stage III Breast Cancer Involving > 10 Axillary Lymph Nodes

KEYWORDS: breast, autologous, bone marrow transplant

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology Oncology

INITIAL APPROVAL DATE: 25 January 1994

### STUDY OBJECTIVE

To determine if adjuvant chemotherapy [four CAF cycles then high-dose combination CPA/CDDP/BCNU with autologous bone marrow support (ABMS)] produces superior disease-free and overall survival compared to adjuvant chemotherapy (four CAF cycles than standard dose CPA/CDDP/BCNU) in patients with Stage II or III breast cancer in 10 or more lymph nodes. Both arms contain Tamoxifen and radiation therapy to chest walls. To compare toxicities experienced between the two programs.

### TECHNICAL APPROACH

Patients entered into this study have pathologically-confirmed Stage II or IIIA breast cancer with  $\geq 10$  lymph nodes involved. The patients are randomized to either of the two treatments. On 6-week schedule they are re-evaluated to determine response to the therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been literature reporting data on this study not previously reported which have now been included (see pubs sect).

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 12. The total number enrolled study-wide is 864, if multi-site study. Grade 4 and Grade 5 toxicities addressed on attached sheets (12pages). Study closed effective May 29, 1998. Adverse events reported Dec 12, 1994, Nov 14, 1995, Mar 28, 1996, Apr 17, 1996, Aug 12, 1996, Sept 24, 1996, Jan 31, 1997, Apr 4, 1997, Jul 30, 1997, Oct 3 1997, and Oct 9, 2002.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early

## DETAIL SUMMARY SHEET

**TITLE:** CALGB 9395 - Phase III Intergroup Study Prospectively Randomized Trial of Perioperative 5-FU after Curative Resection, Followed by 5-FU/Leucovorin for Patients with Colon Cancer

**KEYWORDS:** colon cancer, chemotherapy, Dukes B3 or C

**PRINCIPAL INVESTIGATOR:** Drabick, Joseph COL MC

**ASSOCIATES:**

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Hematology Oncology

**INITIAL APPROVAL DATE:** 25 January 1994

### STUDY OBJECTIVE

To determine if adjuvant therapy with 1 week of 5-fluorouracil given continuously within 24 hours of a curative colon resection followed by 12 months of 5-FU/Levamisole is effective in prolonging disease-free interval and increasing survival in patients with Dukes' B3 or C colon cancer, when compared to patients who are treated with 5-FU/Levamisole only. Endpoints include treatment failure, as defined by recurrence of local/regional or distant metastasis, and survival.

### TECHNICAL APPROACH

All eligible patients will be randomized to receive or not receive 7 days of continuous 5-FU infusion starting within 24 hours of their curative surgery for colon cancer. Those patients found to have evidence of metastatic disease at the time of surgery will be removed from the study. Those patients who have pathologic classification of Dukes' B3 or C colon cancer will receive standard chemotherapy starting 35 days after their surgery; those with Dukes' B1 or 2 will be followed for evidence of recurrence. In December of this year, an addendum to the study was approved by the HUC to include CALGB 9667: Biologic Correlates to Response and Survival in Colon Cancer as a companion to this study; the consent form was modified to include this tissue block study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this protocol since last years review.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 55. The total number enrolled study-wide is 854, if multi-site study. These toxicities were listed as Life Threatening which include 7 leukopenia, 2 granulocytopenia, 3 anemia, 3 infection, 3 nausea, 8 vomiting, 19 diarrhea, 3 stomatitis, 1 liver, 4 pulmonary, 4 cardiac, 1 skin, 6 neuro-motor, 1 neuro-sensory, 2 neuro-clinical, 1 metabolic, and 3 others. Lethal toxicities include 1 other. Adverse events reported Oct 20, 1995, Sept 30, 1996, Jul 17, 1997, Sept 15, 1997, Sept 23, 1997, Sept 30, 1997, Oct 10, 1997, Nov 10, 1997, Dec 11, 1997, Jan 20, 1998, Feb 18, 1998, Apr 6, 1998, Jun 8, 1998, Jul 22, 1998, Nov 23, 1998, Feb 8 1999, Oct 25, 1999, Nov 29, 1999, Mar 8, 2000, Jun 29, 2000, Jul 17, 2000, Sept 18, 2001, Mar 6, 2002, Apr 15, 2002, and May 14, 2002. This study was closed effective May 19, 2000.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9291 - A Randomized Study of Subtotal Nodal Irradiation vs. Irradiation Plus Chemotherapy for Stages I-IIA Hodgkin's disease

KEYWORDS: radiation therapy, chemotherapy, early-stage disease

PRINCIPAL INVESTIGATOR: COL Joseph Drabick MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 26 April 1994

### STUDY OBJECTIVE

To compare the progression-free and overall survival of non-laparotomized patients with clinical stage IA or IIEA Hodgkin's disease treated with subtotal nodal irradiation (3,600 – 4,000 cGy) alone to three cycles of doxorubicin and Vinblastine plus subtotal nodal irradiation.

### TECHNICAL APPROACH

All eligible patients were randomized to receive one of two treatments. Treatment one was 8-9 weeks of daily (x5) radiation therapy. Treatment two was chemotherapy by vein with two drug, doxorubicin and Vinblastine, over 5-10 minutes, every 14 days x 6 doses. The second group received radiation therapy in the same way that treatment one patients received it. All patients were asked to complete a quality-of-life evaluation form before treatment and an additional eight times. The questionnaire took approximately 20-45 minutes to complete. There was a change to the accrual goal, which was reported to the HUC in addendum #8 approved in October 1995.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no new publications reporting data from this study or others with similar study design.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 8. The total number enrolled study-wide is 348, if multi-site study. Grade 4 toxicities include 1 leukopenia, 25 granulocytopenia, 27 maximum grade any toxicity, 1 arrhythmia NOS, 1 dyspnea, 1 hyponatremia, 1 lung-other, 1 mood change, and 1 vomiting. Grade 5 toxicities include 1 pneumonitis, 1 resp inf w/o neut, 1 maximum grade any toxicity, and 1 resp inf with neut. No adverse events reported. This study was closed to accrual effective April 20, 2000.

Ref: CALGB Statistical Report

### CONCLUSIONS

The SWOG DSMC identified that the relapse rate in the chemotherapy plus radiation therapy arm was lower than in the radiation therapy alone arm. However, overall survival was found to be about equal in either arm. WRAMC IRB was informed of these findings in June 2000. This study was published in JCO, November 2001.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9344 - Adjuvant High-Dose vs. Standard-Dose Cyclophosphamide, Adriamycin with/without Taxol for Node-Positive Breast Cancer

KEYWORDS: breast cancer, node positive, adjuvant

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 28 June 1994

### STUDY OBJECTIVE

To determine whether higher doses of doxorubicin used as an adjuvant with cyclophosphamide in patients with early breast cancer will increase disease-free survival and overall survival. To determine whether the use of taxol as single agent after the completion of four cycles of cyclophosphamide and doxorubicin in combination will further improve disease-free and overall survival compared to the two previous drugs alone.

### TECHNICAL APPROACH

All eligible patients will be randomized to one of six treatments: 1) standard dose cyclophosphamide with high-dose doxorubicin followed by taxol; 2) same two initial drugs without taxol; 3) standard cyclophosphamide with moderate dose doxorubicin with taxol afterwards; 4) same two initial drugs without taxol; 5) standard doses of cyclophosphamide and doxorubicin with taxol afterwards; or 6) standard doses without taxol. If taxol is given, there will be four courses. Tamoxifen will be given afterwards to receptor positives. The consent was revised to include new findings on leukemia risk with high-dose therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been an additional publication reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 16. The total number enrolled study-wide is 3170, if multi-site study. Grade 4 toxicities include 327 WBC, 74 platelets, 16 hemoglobin, 711 granulocytes/bands, 484 lymphocytes, 13 nausea, 28 vomiting, 4 diarrhea, 6 stomatitis, esophagitis/dysphasia, 1 anorexia, 1 bilirubin, 1 alkphos 5"NUC, 1 creatinine, 1 BUN, 1 renal failure, 3 dyspnea, 1 other pulmonary, 2 hypotension, 1 embolism, 1 edema, 2 cortical, 1 cerebellar, 2 mood, 1 pain, 1 other neuro, 1 allergy, 5 malaise/fatigue, 1 hyponatremia, 1 prothrombin Time, 1 other mucosal, 4 infection, 1 sensory, and 11 hyperglycemia. Adverse events reported Oct 2, 1995, Mar 25, 1996, Apr 4, 1997, and Jun 16, 1999. This study was closed to accrual effective April 15, 1997.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9394 - A Phase III Comparison of Two Schedules of Cyclophosphamide and Doxorubicin for High-Risk Patients with Breast Cancer Involving 0-3 Axillary Lymph Nodes

KEYWORDS: primary breast cancer, high-risk, 0-3 positive nodes

PRINCIPAL INVESTIGATOR: Joseph Drabick, COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 30 August 1994  
NEW ANNIVERSARY DATE: 30 July

### STUDY OBJECTIVE

To compare disease-free survival, overall survival, and toxicity of high-risk primary breast cancer patients with 0-3 positive axillary lymph nodes treated with adjuvant high-dose chemotherapy with doxorubicin plus cyclophosphamide (AC) or high-dose sequential chemotherapy with doxorubicin followed by cyclophosphamide (AC).

### TECHNICAL APPROACH

All eligible patients will be randomized to one of the two treatment arms as described above. Treatment I will consist of both drugs every 3 weeks times 6 cycles. Treatment II will consist of 4 cycles of doxorubicin at 21-day intervals followed by 3 cycles of cyclophosphamide at 14-day intervals. All post-menopausal and hormone receptor-positive women will then receive Tamoxifen for five years following completion of the chemotherapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been one abstract published that is reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 7. The total number enrolled study-wide is 3176, if multi-site study. This study closed to accrual effective 1 May 1997 and met accrual goal. Grade 4 toxicities included 74 anemia, 2 anxiety/depression, 1 bilirubin increase, 4 cardiac-EF/CHF, 3 cardiac-dysrhythmia, 1 cardiac-other, 2 convulsions, 16 diarrhea, 4 dyspnea, 2 edema, 2 fever without infection, 1 GI, 1 gastritis/ulcer, 705 granulocytopenia, 5 hematologic-other, 1 hemorrhagic cystitis, 1 hypokalemia, 2 hypotension, 4 infection, 732 leukopenia, 355 lymphopenia, 1 mucositis-other, 1 pharynx/esophagitis, 3 phlebitis/thrombosis/embolism, 1 pneumonitis/effusions/infiltr., 1 renal failure, 1 respiratory infection, 1 skin rash/urticaria, 1 stomatitis, 141 thrombocytopenia, 1 transaminase (SGOT, SGPT), 1 vaginal bleeding, 96 vomiting, and 4 miscellaneous-other. Grade 5 toxicities include 1 infection, and 1 miscellaneous-other.

Adverse event memos sent June 9, 1997 and June 18, 1999.  
Ref: CALGB Statistical Report

### CONCLUSIONS

Analysis is in progress.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9351 - A Phase II Study of High-Dose Chemotherapy in Previously Untreated Non-Hodgkin's Lymphoma

KEYWORDS: aggressive disease, high-dose CHOP

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 27 September 1994

### STUDY OBJECTIVE

To: 1) estimate the overall response rate and determine whether dose-intensified CHOP (high-dose CHOP) chemotherapy with G-CSF can be administered with acceptable toxicity to low intermediate-, high intermediate-, and high-risk patients; and 2) determine whether it is possible to identify with early restaging gallium scans a subset of patients who are less likely to achieve a durable complete response.

### TECHNICAL APPROACH

All eligible patients will receive chemotherapy with high doses of cyclophosphamide and doxorubicin and standard doses of vincristine and prednisone. Four cycles will be given at three-week intervals for a total treatment time of three months. G-CSF and an oral antibiotic will be given prophylactically for 14 days after each treatment. The first three days of treatment will be in the hospital; the remainder will be done as an outpatient.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been an abstract reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 4. The total number enrolled study-wide is 99, if multi-site study. Two subjects have died. Grade 4 toxicities include 70 WBC, 65 platelets, 12 hemoglobin, 68 granulocytes/bands, 65 lymphocytes, 1 other hematologic, 1 hemorrhage, 2 infection, 2 diarrhea, 2 stomatitis, 1 esophagitis/dysphagia, 1 anorexia, 3 bilirubin, 1 other liver, 6 hematuria, 1 hemorrhagic cystitis, 3 dyspnea, 2 PO2/PCO2, 1 Ards, 1 dysrhythmia, 1 pain, 2 skin, 1 local, 1 hyperglycemia, 2 hyponatremia, and 1 hypokalemia. Grade 5 toxicity includes 1 other miscellaneous. This study was closed to accrual effective July 31, 1996.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 8642 - A Master Protocol to Study Single-Agent Chemotherapy vs. Standard Chemotherapy for Advanced Breast Cancer

KEYWORDS: chemotherapy, cancer, breast

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 30 June 1987

### STUDY OBJECTIVE

To evaluate ability of single Phase II agents to achieve responses in previously untreated metastatic breast cancer patients.

### TECHNICAL APPROACH

Randomized study in which all eligible patients receive standard cytoxan, Adriamycin and 5-fluorouracil (CAF) therapy, or a Phase II agent. Those randomized to receive a Phase II agent are treated for two cycles and then reevaluated for response or progression. If progression occurs, they are switched to CAF therapy. The next Phase II drug treatment arm, using alsamitruicin, was approved by the CALGB June 1992 for limited institutions.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 18. The total number enrolled study-wide is 365, if multi-site study. Grade 4 toxicities include 62 leukopenia, 26 thrombo, 8 anemia, 5 infection, 6 nausea and vomiting, 1 pulmonary, 2 cardiac, 1 fever w/o infection, 1 local toxicity, 1 hyperglycemia, and 36 other. Grade 5 toxicities include 1 pulmonary. Adverse events reported April 17, 1992, September 7, 1993, March 26, 1996, and September 30, 1996. This study was closed to accrual effective December 31, 1993.

Ref: CALGB Statistical Report

### CONCLUSIONS

This study concluded that in previously untreated metastatic breast cancer patients, the limited use of a single phase II agent prior to treatment with initial standard drugs does not result in any significant increased toxicity, decreased overall response rate, or shortened survival.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9491 – An Intergroup Study of Rectal Cancer Adjuvant Therapy, Phase III

KEYWORDS: 5-Fluorouracil bolus, prolonged infusion, pelvic radiation

PRINCIPAL INVESTIGATOR: Joseph P. Drabick COL MC

ASSOCIATES:

DEPARTMENT: Medicine

SERVICE: Hematology-Oncology

STATUS: O

INITIAL APPROVAL DATE: 25 October 1994

New Anniversary Month: September

### STUDY OBJECTIVE

To compare the effectiveness of 5-FU by bolus injection vs. 5-FU by prolonged infusion given prior to and following combined pelvic radiation therapy plus protracted venous infusion vs. 5-FU by bolus injection plus Leucovorin plus levamisole given prior to and following combined pelvic radiation plus bolus 5-FU plus Leucovorin in the treatment of stage B2, B3, and C rectal cancer.

### TECHNICAL APPROACH

All eligible patients will be randomized to receive one of three treatments: 1) 5-FU bolus for 5 consecutive days, repeated in 4 weeks; 2) continuous 5-FU for 6 weeks intravenously through a portable pump; or 3) 5-FU bolus, similar to treatment 1, but given with levamisole and Leucovorin. Radiation therapy to the pelvis is given in all three treatments. Total treatment time is about 6 months.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this study or from studies with similar study design.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 1917, if multi-site study. Projected accrual was for 2400 patients. Grade 4 toxicities include 15 cardiovascular, 2 dermatologic, 82 gastrointestinal, 279 hematologic, 11 infection, 1 lung, 3 metabolic, 1 musculoskeletal, 5 neurologic, 4 renal/bladder, and 1 secondary malignancy. Grade 5 toxicities include 3 cardiovascular, 2 gastrointestinal, 1 hemorrhage, 7 infection, and 3 lung. This study was closed to accrual effective August 1, 2000 – met accrual goals.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.



## DETAIL SUMMARY SHEET

TITLE: CALGB 9497 – Health Status and Quality-of-Life in Patients with Early Stage Hodgkin's Disease;  
A Companion Study to CALGB 9391

KEYWORDS: quality-of-life, early stage, Hodgkin's

PRINCIPAL INVESTIGATOR: Joseph P. Drabick COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 25 October 1994  
New Anniversary Month: September

### STUDY OBJECTIVE

To evaluate prospectively the health status and quality-of-life (QOL) of early-stage Hodgkin's disease patients receiving either subtotal nodal irradiation or short-course chemotherapy plus subtotal nodal irradiation. To describe the short-term, acute effects of two treatments for early-stage disease on patient reports of symptoms of QOL.

### TECHNICAL APPROACH

All patients eligible for treatment on the treatment study CALGB # 9391 will be registered to this companion study and complete questionnaires related to current health status and QOL. These questionnaires will be completed prior to treatment and at eight specified time points during their treatment. The results will be reviewed and analyzed by the Psycho-Oncology Committee at CALGB.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have not been any publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 8. The total number enrolled study-wide is 263, if multi-site study. This study was closed to accrual effective April 20, 2000.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9343 - Evaluation of Lumpectomy, Tamoxifen, and Irradiation of the Breast Compared with Lumpectomy plus Tamoxifen in Women 70 Years of Age or Older Who Have Carcinoma of the Breast That Is Less Than or Equal to 4 Cm and Clinically- Negative Axillary Nodes

KEYWORDS: Tamoxifen, breast, lumpectomy

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 29 November 1994

### STUDY OBJECTIVE

To determine the net value of radiation therapy in eligible patients with breast cancer, all of who receive Tamoxifen. To assess whether radiation therapy decreases rate of recurrence and incidence of eventual mastectomy. To estimate overall survival, disease-free survival, and breast cancer-specific morbidity for the two groups.

### TECHNICAL APPROACH

Eligible breast cancer patients will be randomized to receive either a lumpectomy followed by Tamoxifen, or lumpectomy followed by radiation therapy (for approximately 6 weeks) plus Tamoxifen. Patients will be followed closely for recurrence. In the event of mastectomy subsequent to initial lumpectomy, patients will go off study and be followed for second primary and mortality.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review a year ago, there have been no publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 13. The total number enrolled study-wide is 647, if multi-site study. There have been no toxicities reported on this study. This study was closed to accrual effective 26 February 1999. Adverse events reported 4 April 1997 and 22 September 1998.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9312 - Phase III Comparison of Standard vs. Myeloablative Therapy for Previously Untreated Symptomatic Multiple Myeloma

KEYWORDS: myeloma, transplant, interferon

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 20 December 1994

### STUDY OBJECTIVE

1) To perform a randomized trial in newly diagnosed systemic myeloma (MM) patients, of standard therapy vs. myeloablative therapy in order to examine whether intensive therapy translates into extended survival and progression-free survival. 2) To randomize responding patients to interferon vs. no maintenance to evaluate the role of interferon in MM.

### TECHNICAL APPROACH

All eligible patients will receive standard chemotherapy (vincristine, doxorubicin, and dexamethasone) for 4 cycles. Responding patients will be randomized to receive autologous stem cell transplant with high dose chemotherapy or standard chemotherapy for 12 months. All patients will initially receive high-dose Cytosan before transplant. After completion of transplant or chemotherapy, all patients will be randomized to observation or maintenance with interferon. This study has been amended several times this year to afford all patients the opportunity of bone marrow transplantation at some point in their treatment.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this study or from studies with similar study design.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 22. The total number enrolled study-wide is 899, if multi-site study. Grade 4 toxicities include 15 cardiovascular, 4 dermatologic, 1 endocrine, 5 flu-like symptoms, 56 gastrointestinal, 503 hematologic, 4 hemorrhage, 1 immunological, 13 infection, 22 lung, 38 metabolic, 16 neurologic, 6 pain, 18 renal/bladder, 4 infection, 2 liver, 1 miscellaneous, 2 syndromes, and 1 secondary malignancy. Grade 5 toxicities include 4 ADR, 4 cardiovascular, 1 gastrointestinal, 2 hemorrhage, 22 infection, 7 lung, 3 renal/bladder, 9 infection, and 2 syndromes. Adverse events memo sent to Col Sjogren from Hem Onc ref. SWOG Memo dated Sept 6, 1995 (microangiopathic renal failure). Additional memos sent from Hem Onc dated Apr 2, 1996, Jun 4, 1996, Dec 2, 1996, Jan 2, 1997, Apr 17, 1996, Apr 23, 1997, Jun 25, 1997, Aug 11, 1997, Sept 22, 1997, May 19, 1998, Nov 3, 1998, Feb 23, 1999, Jun 23, 1999, Sept 9, 1999, Sept 29, 1999, Sept 11, 2000, Jan 9, 2001, and Aug 9 2001. This study was closed to accrual effective 1 October 2000.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9498 - A Phase III Randomized Trial of 5-FU/Levamisole/Fluovorin vs.5-FU/Levamisole as Adjuvant Therapy for Colon Cancer

KEYWORDS: colon cancer, levamisole, leucovorin

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology Oncology

INITIAL APPROVAL DATE: 31 January 1995

### STUDY OBJECTIVE

To compare the effectiveness of bolus 5-FU/leucovorin/levamisole vs. continuous infusion 5-FU/levamisole as adjuvant therapy for patients with Stage B2, C1, or C2 colon cancer. This will be measured in terms of overall survival. Disease-free survival will be secondary endpoint.

### TECHNICAL APPROACH

Eligible patients will be randomized to either bolus 5-FU/leucovorin/levamisole or to infusion 5-FU/levamisole. In arm 1, cycles will be repeated at the end of 4 weeks, 8 weeks, and then every 5 weeks for a total of 6 cycles; levamisole will continue for 6 months. In arm 2, following each of the initial 2-week cycles, there will be a 1-week rest followed by a resumption of chemotherapy. Patients with progressive disease or unacceptable toxicities will be removed from the study. All patients will be followed until death.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this study or from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 1135, if multi-site study. Grade 4 toxicities include 5 cardiovascular, 1 clotting, 1 flu-like symptoms, 41 gastrointestinal, 115 hematologic, 3 infection, 1 liver, 2 lung, 3 metabolic and 4 pain. Grade 5 toxicity includes 2 infection. No adverse events reported. This study closed December 15, 1999.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9511 - A Pilot Trial with Limited Pharmacokinetic Monitoring During Remission Induction and Consolidation Chemotherapy for Adult Acute Lymphoblastic Leukemia

KEYWORDS: PEG-Asparaginase, pharmacokinetic, ALL

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 29 August 1995

### STUDY OBJECTIVE

- 1) Determine toxicity profile for PEG-Asparaginase given as part of intensive multi-agent chemotherapy in patients with previously untreated ALL;
- 2) Determine incidence and significance of neutralizing antibodies, and levels of asparaginase after early treatment with PEG-Asparaginase; and
- 3) Obtain estimate of relationship of these to outcome in ALL.

### TECHNICAL APPROACH

Eligible consenting patients with previously untreated ALL will receive aggressive chemotherapy that includes PEG-Asparaginase in place of L-Asparaginase during induction and early intensification phases of treatment (lasting 60 days), and standard chemotherapy for remaining phases of treatment (lasting 2 years). Patients will be monitored weekly during maintenance therapy, every 3 months for the following year if the patient is in remission, and every 6 months for 4 additional years.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been additional publications since last APR reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 6. The total number enrolled study-wide is 104, if multi-site study.

Study closed to accrual effective December 15, 1997, because it met its accrual goal. Grade 5 toxicities include 1 infection, 1 adult respiratory distress syndrome (ARDS), 4 infections, 1 hepatic, 1 pulmonary, 1 renal.

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9251 - A High Intensity, Brief Duration Phase II Chemotherapy Trial in Small, Non-Cleaved Lymphoma and L-3 Acute Lymphoblastic Leukemia (ALL)

KEYWORDS: high intensity, Phase II, chemotherapy

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 28 November 1995

### STUDY OBJECTIVE

To determine: 1) response rate and disease-free survival of patients with category "J" NHL and L3 ALL, not associated with HIV infection, when treated with high intensity, brief duration chemotherapy; and 2) toxicity of this regimen in an HIV-negative patient population.

### TECHNICAL APPROACH

All eligible patients will receive the same therapy. All drugs have been used previously to treat these diseases, but will be given at higher doses for a shorter time period. Course I (day 1-7) includes CPA (IV) and prednisone (po). Course II (day 8-12) includes IFF, Mesna, MTX, Leuco, VCR, Ara-C, Etop (IV), Dex (po), and intrathecal combination chemotherapy (day 8 and 12). This therapy is repeated for Course VI (day 50-54) and Course IV (day 92-96). Course III (day 29-33) includes CPA, MTX, Leuco, VCR, Adr (IV), Dex (po), and intrathecal combination chemotherapy (day 29 and 31). This is followed by cranial radiation therapy on days 34 to 49 in Course III only. Course III chemotherapy is repeated for Course V (day 71-75) and Course VII (day 113-117). All patients will receive first three courses at full dose and on time. In event of slow marrow recovery, later doses may be delayed.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There is one publication reporting data on this protocol.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 134, if multi-site study. Grade 4 toxicities include 121 WBC, 108 platelets, 34 hemoglobin, 118 granulocytes, 113 lymphocytes, 6 other hematologic, 5 hemorrhage, 16 infection, 5 vomiting, 5 diarrhea, 35 stomatitis, 17 esophagitis/dysph, 11 anorexia, 2 other GI, 3 other mucosal, 12 bilirubin, 3 transaminase, 3 other liver, 1 creatinine, 2 hematuria, 3 BUN, 2 hemorrhagic cyst, 5 renal failure, 7 dyspnea, 1 PO2/PCO2, 6 pulmonary edema, 3 Ards, 5 other pulmonary, 5 dysrhythmia, 1 cardiac function, 1 other heart, 4 hypotension, 4 edema, 1 sensory, 4 motor, 2 cortical, 2 mood, 8 pain, 1 other neurologic, 1 skin, 1 local, 1 fever w/o infect, 1 myalgias/arthritis, 10 malaise/fatigue, 2 hyperglycemia, 1 hypoglycemia, 1 amylase, 2 hypercalcemia, 8 hypocalcemia, 1 hypomagnesemia, 2 hyponatremia, 3 hypokalemia, 1 fibrinogen, 2 prothrombin time, 7 partial thromboplastin, 1 eye, and 5 other misc. Grade 5 toxicities include 1 lymphocyte, 7 infections, and 1 other pulmonary, and 1 dysrhythmia. This study closed to accrual effective 29 February 2000.

Ref: CALGB Statistical Report

### CONCLUSIONS

Preliminary results show this therapy to be associated with a high response rate and durable remissions. No final conclusions have been reached.

## DETAIL SUMMARY SHEET

TITLE: Cancer and Leukemia Group B

KEYWORDS: grant, NIH, cancer

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC

ASSOCIATES:

DEPARTMENT: Medicine

SERVICE: Hematology-Oncology

STATUS: O

INITIAL APPROVAL DATE: 25 January 1996  
Umbrella Study

### STUDY OBJECTIVE

This is the NIH "umbrella" grant for all CALGB studies at WRAMC. CALGB brings together more than two dozen academic institutions and their affiliates in order to conduct cancer treatment trials and related research.

### TECHNICAL APPROACH

At WRAMC, through the CALGB program, over thirty active protocols are available to eligible DOD patients. All WRAMC protocol patients are followed by CALGB staff for life regardless of status of protocol enrollment. Patients are treated per individual protocol.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

During this reporting period, WRAMC has maintained steady enrollment to active protocols, new protocol submissions in many areas of oncology research, timely and complete patient follow-up, and up to date continuing review on all open protocols. CALGB researchers' at WRAMC continue to participate in CALGB national meetings, serve on CALGB committees, publish in their fields, and provide appropriate study information to the staff and patients at WRAMC. NNMC remains an affiliate of WRAMC. Please see individual protocols.

### CONCLUSIONS

CALGB continues to be a healthy and growing research organization at WRAMC aspiring to provide the best study opportunities for our patients that desire them.

## DETAIL SUMMARY SHEET

TITLE: CALGB 8762 - Molecular Subtypes in Acute Lymphatic Leukemia with Philadelphia Chromosome

KEYWORDS: Philadelphia chromosome, ALL

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 27 October 1987

### STUDY OBJECTIVE

To determine the incidence of pH positivity in patients with previously untreated acute lymphatic leukemia (ALL).

### TECHNICAL APPROACH

Non-randomized comparison study in which all eligible patients who consent allow a sample of blood and bone marrow to be sent to a reference laboratory at the time of diagnosis, first intensification, and at relapse.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 15. The total number enrolled study-wide is 393, if multi-site study. No grade 4 toxicities reported. Adverse events reports sent September 16, 1996, and September 22, 1997. This study was closed to accrual effective April 15, 1999.

Ref: CALGB Statistical Report

### CONCLUSIONS

While final conclusions have not been reached, analysis is ongoing and has shown correlation between chromosomal features and disease outcome and response to treatment.



## DETAIL SUMMARY SHEET

TITLE: CALGB 8762 – Molecular Subtypes in Acute Lymphatic Leukemia with Philadelphia Chromosome

KEYWORDS: Philadelphia chromosome, ALL

PRINCIPAL INVESTIGATOR: Joseph P. Drabick COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 27 October 1987

New Anniversary Month: September

### STUDY OBJECTIVE

To determine the incidence of pH positivity in patients with previously untreated acute lymphatic leukemia (ALL).

### TECHNICAL APPROACH

Non-randomized comparison study in which all eligible patients who consent allow a sample of blood and bone marrow to be sent to a reference laboratory at the time of diagnosis, first intensification, and at relapse.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 15. The total number enrolled study-wide is 393, if multi-site study. No Grade 4 toxicities reported. Adverse event reports sent September 16, 1996, and September 22, 1997. The study closed to accrual effective April 15, 1999.

Ref: CALGB Statistical Report

### CONCLUSIONS

While final conclusions have not been reached, analysis is ongoing and has shown correlation between chromosomal features and disease outcome and response to treatment.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9334 - Sclerosis of Pleural Effusions by Talc Thoracoscopy vs. Talc Slurry: A Phase III Study

KEYWORDS: Pleural Effusion, Talc Slurry, Thoracoscopy  
PRINCIPAL INVESTIGATOR: COL Joseph Drabick MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 23 April 1996

### STUDY OBJECTIVE

To compare a proportion of patients with successful pleurodesis at 30 days post-treatment for malignant pleural effusion (MPE) by talc slurry via chest tube or thorascopic talc insufflations. To compare the cost of treating MPE patients with these methods. To compare treatments with respect to time to recurrence of effusion, duration of drainage, extent of post treatment complications and toxicities, and patient quality-of-life and pain.

### TECHNICAL APPROACH

Eligible patients with MPE will be randomly assigned to receive either thoracoscopy with talc insufflations or talc slurry via chest tube at the bedside. Patients will be closely monitored for medical and surgical complications for 30 days, and actively followed for six months. Patients will complete quality-of-life instruments before treatment and 30 days after treatment. Pain will be assessed 2x per day while patient has a chest tube in place after procedure. Monthly follow-up visits with chest x-rays will be done for six months.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been a publication reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 12. The total number enrolled study-wide is 501, if multi-site study. Grade 4 toxicities include 2 WBC, 2 granulocytes/bands, 4 lymphocytes, 22 dyspnea, 4 PO2/PCO2, 4 pulmonary edema, 3 Ards, 4 other pulmonary, 3 dysrhythmia, 2 cardiac function, 1 ischemia, 2 hypotension, 1 cortical, 4 malaise/fatigue, 1 partial thromboplast, 1 other miscellaneous, and 22 maximum toxicity. Adverse events reported Oct 21, 1996, Mar 6, 1997, May 7, 1998, Dec 29, 1998, Jan 7, 1999, Feb 22, 1999, Mar 1, 1999, Mar 25, 1999, May 13, 1999, and Apr 26, 2000. Study closed to accrual effective September 30, 1999.

Ref: CALGB Statistical Report

### CONCLUSIONS

Analysis ongoing. Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9334 - Sclerosis of Pleural Effusions by Talc Thoracoscopy vs. Talc Slurry: A Phase III Study

KEYWORDS: Pleural Effusion, Talc Slurry, Thoracoscopy

PRINCIPAL INVESTIGATOR: COL Joseph Drabick MC

DEPARTMENT: Medicine

STATUS: C

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 23 April 1996

### STUDY OBJECTIVE

To compare a proportion of patients with successful pleurodesis at 30 days post-treatment for malignant pleural effusion (MPE) by talc slurry via chest tube or thoracoscopic talc insufflations. To compare the cost of treating MPE patients with these methods. To compare treatments with respect to time to recurrence of effusion, duration of drainage, extent of post treatment complications and toxicities, and patient quality-of-life and pain.

### TECHNICAL APPROACH

Eligible patients with MPE will be randomly assigned to receive either thoracoscopy with talc insufflations or talc slurry via chest tube at the bedside. Patients will be closely monitored for medical and surgical complications for 30 days, and actively followed for six months. Patients will complete quality-of-life instruments before treatment and 30 days after treatment. Pain will be assessed 2x per day while patient has a chest tube in place after procedure. Monthly follow-up visits with chest x-rays will be done for six months.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been a publication reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 12. The total number enrolled study-wide is 501, if multi-site study. Grade 4 toxicities include 2 WBC, 2 granulocytes/bands, 4 lymphocytes, 22 dyspnea, 4 PO2/PCO2, 4 pulmonary edema, 3 Ards, 4 other pulmonary, 3 dysrhythmia, 2 cardiac function, 1 ischemia, 2 hypotension, 1 cortical, 4 malaise/fatigue, 1 partial thromboplast, 1 other miscellaneous, and 22 maximum toxicity. Adverse events reported Oct 21, 1996, Mar 6, 1997, May 7, 1998, Dec 29, 1998, Jan 7, 1999, Feb 22, 1999, Mar 1, 1999, Mar 25, 1999, May 13, 1999, and Apr 26, 2000. Study closed to accrual effective September 30, 1999. CALGB is no longer collecting data on the study participants. WRAMC is closing this study.

### CONCLUSIONS

Analysis is ongoing. Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 8763 - Immunoglobulin and T Cell Receptor Gene Rearrangement in Adult Acute Lymphatic Leukemia

KEYWORDS: immunoglobulin, T-cell receptor, ALL

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 27 October 1987

### STUDY OBJECTIVE

To determine the incidence of Ig and T-cell receptor gene rearrangements from samples of patients with previously untreated adult acute lymphatic leukemia (ALL).

### TECHNICAL APPROACH

Non-randomized companion study in which all eligible patients who consent allow a sample of bone marrow and blood to be sent to CALGB reference laboratory at the time of diagnosis, prior to first intensification, and at relapse.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been one published abstract reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 10. The total number enrolled study-wide is 370, if multi-site study. No grade 4 toxicities reported. This study was closed to further accrual effective May 31, 1996 – met its objectives. Adverse event reported September 16, 1996, and September 22, 1997.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 8763 – Immunoglobulin and T Cell Receptor Gene Rearrangement in Adult Acute Lymphatic Leukemia

KEYWORDS: immunoglobulin, T-cell receptor, ALL

PRINCIPAL INVESTIGATOR: Joseph P. Drabick COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 27 October 1987  
New Anniversary Month: September

### STUDY OBJECTIVE

To determine the incidence of Ig and T-cell receptor gene rearrangements from samples of patients with previously untreated adult acute lymphatic leukemia (ALL).

### TECHNICAL APPROACH

Non-randomized companion study in which all eligible patients who consent allow a sample of bone marrow and blood to be sent to CALGB reference laboratory at the time of diagnosis, prior to first intensification, and at relapse.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

I have found no additional publications reporting any data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 10. The total number enrolled study-wide is 370, if multi-site study. No grade 4 toxicities reported. Adverse events reported September 16, 1996 and September 22, 1997. Study was closed to accrual effective May 31, 1996 (met its objective).

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 8361 - Immunologic Diagnostic Studies in AML (Blood Drawing Phase; Previously CALGB 7921); A Comparative Study of Three Remission Induction Regimens and Two Maintenance Regimens for AML (Treatment Phase; Previously CALGB 8321)

KEYWORDS: immunology, oncology, leukemia

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 31 December 1981

### STUDY OBJECTIVE

1) To determine the incidence of various markers in acute myelogenous leukemia (AML); 2) To correlate the presence of these markers and the surface antigen phenotype they determine with the FAB histological classification; and 3) To correlate the presence of the various markers with the initial and subsequent clinical characteristics of the disease.

### TECHNICAL APPROACH

All eligible patients are registered prior to the initial therapy. From the diagnostic bone marrow procedure, 2 cc of bone marrow and 7 cc of peripheral blood are collected and sent by express mail to the CALGB reference laboratory for analysis and confirmation of classification. Samples are again obtained at relapse.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been literature published reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 65. The total number enrolled study-wide is 2405, if multi-site study. Study was closed to accrual 30 May 1997 after meeting study objective.

Ref: CALGB Statistical Report

### CONCLUSIONS

Immunophenotyping has provided useful in the stratification of some leukemia at high risk for relapse. Analysis is ongoing.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9254 - Anti-B4-Blocked-Ricin (NSC #639185) Adjuvant Post-Autologous Bone Marrow Transplant - A Phase III Study

KEYWORDS: ABB, ricin, NHL

PRINCIPAL INVESTIGATOR: Joseph P. Drabick COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 28 May 1996

### STUDY OBJECTIVE

To determine the effect on disease-free survival of Anti-B4-bR administered by 7-day continuous infusion to patients in complete remission after ABMT for B-cell NHL.

### TECHNICAL APPROACH

All eligible NHL patients who consent to this study will receive standard ABMT therapy. If they achieve complete remission, they will be randomized to receive Anti-B4-Blocked-Ricin or observation. Patients who receive ABB will receive a 7-day continuous infusion between 60 and 120 days post ABMT, and another course 14 days later. Treatment is done on an outpatient basis with frequent (6 visits) clinic monitoring. Lab studies are routine for ABMT patients with 1 extra tube for pharmacokinetic samples in patients receiving drug treatment. Patients will be followed by clinic visits every 6 months for 3 years.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been a publication reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 511, if multi-site study. Grade 4 toxicities include 1 WBC, 5 platelets, 3 granulocytes/bands, 21 lymphocytes, 2 dyspnea, 1 non-infect. pneumoni, 1 Ards, 1 dysrhythmias, 1 other heart, 1 hypotension, 2 edema, 1 pain, 1 skin, 1 malaise/fatigue and 1 hypocalcemia. No adverse events reported. This study closed to accrual effective March 18, 1997.

Ref: CALGB Statistical Report

### CONCLUSIONS

Study closed because it would show no significant benefit to patients to continue to its original accrual goal.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9254 - Anti-B4-Blocked-Ricin (NSC #639185) Adjuvant Post-Autologous Bone Marrow Transplant - A Phase III Study

KEYWORDS: ABB, ricin, NHL

PRINCIPAL INVESTIGATOR: Joseph P. Drabick COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: C  
INITIAL APPROVAL DATE: 28 May 1996

### STUDY OBJECTIVE

To determine the effect on disease-free survival of Anti-B4-bR administered by seven-day continuous infusion to patients in complete remission after ABMT for B-cell NHL.

### TECHNICAL APPROACH

All eligible NHL patients who consent to this study will receive standard ABMT therapy. If they achieve complete remission, they will be randomized to receive Anti-B4-Blocked-Ricin or observation. Patients who receive ABB will receive a seven-day continuous infusion between 60 and 120 days post ABMT, and another course fourteen days later. Treatment is done on an outpatient basis with frequent (six visits) clinic monitoring. Lab studies are routine for ABMT patients with one extra tube for pharmacokinetic samples in patients receiving drug treatment. Patients will be followed by clinic visits every six months for three years.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been a publication reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 511, if multi-site study. Grade 4 toxicities include 1 WBC, 5 platelets, 3 granulocytes/bands, 21 lymphocytes, 2 dyspnea, 1 non-infect. Pneumoni, 1 Ards, 1 dysrhythmia, 1 other heart, 1 hypotension, 2 edema, 1 pain, 1 skin, 1 malaise/fatigue and 1 hypocalcemia. No adverse events reported. This study closed to accrual effective March 18, 1997. CALGB no longer requires any data collection from patients on this study. WRAMC is closing the study.

### CONCLUSIONS

Study closed to accrual because it would show no significant benefit to patients to continue to its original accrual goal.



## DETAIL SUMMARY SHEET

TITLE: CALGB 9665 - The CALGB Leukemia Tissue Bank

KEYWORDS: leukemia, tissue bank

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 25 June 1996

### STUDY OBJECTIVE

To collect and store specimens from every newly diagnosed patient with acute leukemia or myelodysplasia syndrome (MDS) who is entered on a CALGB protocol for previously untreated patients.

### TECHNICAL APPROACH

All consenting eligible patients with newly diagnosed leukemia or MDS entered on a CALGB treatment protocol will have blood, bone marrow, and cell samples collected as follows: 1) pre-treatment - bone marrow aspirate (5 cc), blood (8-10 cc), 2 buccal swab samples (by twirling special brush inside cheek for 30 seconds); 2) during remission - similar blood and bone marrow samples at intervals specified in treatment protocol; and 3) at relapse - similar blood and bone marrow specimens x 1. All samples will be sent per protocol to CALGB Tissue Bank at Roswell Park Cancer Institute for use in further studies (no heritable genes).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been several publications reporting data on this study. See attached sheets.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 30. The total number enrolled study-wide is 1922, if multi-site study. This is a tissue banking study.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 8852 - A Study of CHOPE in Diffuse Lymphomas

KEYWORDS: lymphoma, CHOPE, high-dose

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology Oncology

INITIAL APPROVAL DATE: 31 January 1989

### STUDY OBJECTIVE

To identify the maximum tolerated dose of cyclophosphamide, doxorubicin, vincristine, prednisone, and etoposide (CHOPE) in the treatment of lymphoma, and to assess the safety of giving multiple cycles of high-dose CHOPE therapy

### TECHNICAL APPROACH

Standard doses of CHOPE will be given to the first 20-25 patients enrolled. If tolerated, the doses will be escalated for the next groups sequentially, until the maximum tolerated dose is reached.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no additional publications reported on this study (just consolidation of previously reported literature).

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 5. The total number enrolled study-wide is 227, if multi-site study. Grade 4 toxicities include 174 leukopenia, 64 thrombo, 203 granulocytopenia, 19 anemias, 13 infections, 3 GU, 3 hepatic, 5 nausea and vomiting, 7 other GI, 6 pulmonary, 1 cardiac, 2 neurologic cns, 1 skin, 1 allergy, 1 fever w/o infection, 5 other-1, and 1 other-2. Grade 5 toxicities include 3 infection, 2 cardiac, 1 GU, 1 hepatic, and 1 cardiac. No adverse events reported. This study closed effective May 24, 1993.

Ref: CALGB Statistical Report

### CONCLUSIONS

Analysis is in progress.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9583 - A Phase III Two-Arm Randomized Study Comparing Antiandrogen Withdrawal vs. Antiandrogen Withdrawal Combined with Ketoconazole and Hydrocortisone in Patients with Advanced Prostate Cancer

KEYWORDS: advanced, prostate cancer, ketoconazole

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology Oncology

INITIAL APPROVAL DATE: 28 January 1997

### STUDY OBJECTIVE

To compare the response proportion and duration of response to antiandrogen withdrawal alone vs. antiandrogen withdrawal combined with ketoconazole and hydrocortisone in patients with advanced hormone refractory prostatic carcinoma

### TECHNICAL APPROACH

All eligible, consenting men will be randomly assigned to #1 stop flutamide or Casodex or #2 stop Flutamide or Casodex and start treatment with ketoconazole po tid and hydrocortisone po bid. Patients entering this will also have a bone marrow biopsy done as part of companion study CALGB 9663 (consented separately). Treatment is outpatient with clinic visits every 4 weeks. Study treatment will continue until there is clinical evidence that it is no longer effective.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no additional publications reporting data since last years report.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 4. The total number enrolled study-wide is 260, if multi-site study. Grade 4 toxicities include 1 vomiting, 1 other mucosal, 3 dyspnea, 1 other pulmonary, 1 cardiac function, 1 pericardial, 1 other heart, 1 mood, 2 other neurologic, 1 hyperglycemia, 1 amylase, 1 hypercalcemia, 1 hypocalcemia and 1 prothrombintine. Adverse events reported Dec 6, 2000, Jan 12, 2001 and May 21, 2001. This study was closed effective May 31, 2000.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9760 - Multidrug Resistance Studies in Acute Leukemia

KEYWORDS: resistance, multidrug, AML

PRINCIPAL INVESTIGATOR: LTC Joseph J. Drabick MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 24 June 1997

### STUDY OBJECTIVE

To study Pgp antigen expression in MDR in patients with acute leukemia at diagnosis, relapse and refractory disease. To correlate Pgp mediated MDR with pretreatment patient characteristics. To study PSC-833 Pgp modulation. To study MDR mediated by other mediators including MRP and LRP. To determine frequency of Pgp, MRP and LRP mediated MDR in adult leukemic cells, and correlate with pretreatment characteristics and with treatment outcome.

### TECHNICAL APPROACH

Bone marrow and/or peripheral blood samples as specified in the protocol are collected from consenting patients with acute leukemia at the time of diagnosis (before treatment), and at time of relapse or diagnosis of refractory disease. These samples are taken at times when the procedure is already being carried out for standard diagnostic care. The laboratory results are then correlated with clinical outcome.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There was a publication reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 14. The total number enrolled study-wide is 907, if multi-site study. There have been no adverse events reported.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 8961 - RAS Mutations in Myelodysplasia

KEYWORDS: RAS gene, oncogenes, myelodysplasia

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 25 April 1989

### STUDY OBJECTIVE

To determine 1) the prevalence of mutant RAS genes in myelodysplasia; 2) if the presence of such a mutation predicts subsequent leukemic development.

### TECHNICAL APPROACH

Non-randomized, non-treatment protocol in which all eligible patients are registered. Blood and bone marrow samples and slides are obtained at entry and again, when acute leukemia develops.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No change in publications reported.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 13. The total number enrolled study-wide is 308, if multi-site study. No grade 4 toxicities reported. Adverse event reported May 3, 2002. Study was closed to accrual effective 30 September 1996.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9640 - A Comparison of Intensive Sequential Chemotherapy Using Doxorubicin Plus Paclitaxel Plus Cyclophosphamide with High-Dose Chemotherapy and Autologous Hematopoietic Progenitor Cell Support for Primary Breast Cancer in Women with 4-9 Involved Axillary Lymph Nodes

KEYWORDS: chemotherapy, breast, progenitor cell support

PRINCIPAL INVESTIGATOR: Joseph Drabick COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 29 July 1997

### STUDY OBJECTIVE:

To compare induction chemotherapy followed by high dose chemo and autologous stem cell support vs. intensive sequential chemo with G-CSF support with respect to disease free survival, toxicity and overall survival in operable patients with 4-9 positive nodes.

### TECHNICAL APPROACH

Eligible women will be randomly assigned to receive either 1) high-dose chemo with doxorubicin, paclitaxel and cyclophosphamide over seventeen weeks with G-CSF support; or 2) standard dose chemo over ten weeks, followed by higher dose chemo with cyclophosphamide, thiotepa, and carboplatin with autologous stem cell collection after week ten, and reinfusion four days after completion of high dose chemo. Both groups will be given radiation treatment 4-6 weeks post therapy, and tamoxifen therapy for five years.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this study's last review there have been no publications reporting data on this protocol.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 590, if multi-site study. Grade 4 toxicities include 1 ARDS, 21 anemia, 1 dizziness/light headedness, 2 dizziness/vertigo, NOS, 3 dyspnea, 1 fatigue/malaise/lethargy, 5 febrile neutropenia, 2 GU-other, 2 infection w/o 3-4 neutropenia, 1 infection with 3-4 neutropenia, 1 infection, unk ANC, 2 LVEF decrease/CHF, 353 leukopenia, 4 myalgia/arthralgia, NOS, 368 neutropenia/granulocytopenia, 2 platelet transfusion, 1 pulmonary edema, 1 respiratory infect w/neutrop, 11 stomatitis/pharyngitis, 66 thrombocytopenia, 3 thrombosis/embolism, 8 vomiting, 1 confusion, 6 anorexia, 1 diarrhea w/o colostomy, 2 esophagitis/dysphagia, 1 fever w/o neutropenia, 1 fever, NOS, 1 hyperglycemia, 1 hypertension, 1 hypocalcemia, 1 hypokalemia, 1 hypotension, 1 liver-other, 1 mood/consciousness chg, NOS, 2 renal failure, 1 SGOT (AST) increase, 1 second primary, 1 supraventricular arrhythmia, 1 thrombotic microangiopathy, 1 ventricular arrhythmia. Grade 5 toxicities include 1 ARDS, 1 cardiovascular-other, 2 infections with 3-4 neutropenia, 1 infection w/o 3-4 neutropenia, 1 respiratory infect w/o neutrop, and 1 veno-occlusive disease. No adverse events reported. This study was closed to accrual effective February 15, 2001.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9621 - Phase I Study of MDR Modulation with PSC-833 with a Pilot Study of Cytogenetic Risk-Adapted Consolidation Followed by a Phase II Pilot Study of Immunotherapy with rIL-2 in Previously Untreated Patients with AML < 60 Years

KEYWORDS: PSC-833, MDR Modulation, rIL-2

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 26 August 1997

### STUDY OBJECTIVE

To determine the MTD for the intensive chemotherapy used in the study. To establish the feasibility and toxicity of administering post remission therapy in a risk adapted fashion. To establish feasibility of maintenance therapy with rIL-2.

### TECHNICAL APPROACH

Eligible patients with AML will receive standard induction chemotherapy plus minus PSC-833 followed by risk stratified therapy with either stem cell transplant or intensive chemotherapy, followed by immunotherapy with rIL-2. Therapy duration is 24 weeks. Patients will be followed for life.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been several publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 10. The total number enrolled study-wide is 410, if multi-site study.

This study was closed to enrollment effective March 31, 2000. Grade IV toxicities include 2 hemorrhage, 30 infection, 2 vomiting, 13 diarrhea, 75 stomatitis, 57 esophagitis, 24 anorexia, 6 other GI, 72 bilirubin, 2 other liver, 5 transaminase, 2 BUN, 38 dyspnea, 15 pulm. edema, 4 other pulmonary, 18 ARDS, 25 dysrhythmia, 2 ischemia, 25 hypotension, 1 cortical, 9 pain, 16 skin, 10 fever w/o infect., 28 malaise/fatigue, 3 hyperglycemia, 11 hypocalcemia, 7 hypokalemia, and 1 other metabolic. Grade V toxicities include 3 hemorrhage, 18 infection, 1 other GI, 6 ARDS, 1 ischemia, 1 cortical, 1 other metabolic, and 2 other pulmonary.

Adverse event memos have been sent to DCI on 3/23/98, 9/24/98, 4/21/00, 7/11/00, 9/15/00, 1/12/01, 11/28/01, 12/5/01, and 5/3/02.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 8952 - Combination Chemotherapy for Advanced Hodgkin's Disease, Phase III

KEYWORDS: chemotherapy, Hodgkin's disease

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 29 August 1989

### STUDY OBJECTIVE

To compare ABVD to the MOPP/ABV hybrid as therapy for patients with Hodgkin's disease in terms of complete response rates, disease-free survival, failure-free survival, and both intermediate and long-term toxicities.

### TECHNICAL APPROACH

Randomized study in which eligible patients receive either ABVD or the MOPP/ABV hybrid combination for a minimum of six cycles unless progression is documented.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been an additional publication reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 9. The total number enrolled study-wide is 856, if multi-site study. Grade IV toxicities include 212 wbc, 38 platelets, 31 hemoglobin, 324 granulocytes/bands, 311 lymphocytes, 4 other hematologic, 1 hemorrhage, 11 infection, 10 vomiting, 2 diarrhea, 1 anorexia, 2 other GI, 4 bilirubin, 6 transaminase, 1 alk phos/5' nucleot, 1 liver-clinical, 1 creatinine, 1 hematuria, 1 renal failure, 11 dyspnea, 7 po2/pco2, 2 dlco, 1 fibrosis, 1 pulmonary edema, 6 non-infect. pneumon., 6 ARDS, 3 other pulmonary, 3 dysrhythmia, 2 cardiac function, 1 ischemia, 4 other heart, 4 hypotension, 3 phlebitis/thrombosis, 1 edema, 1 sensory, 1 motor, 1 cortical, 3 mood, 1 constipation, 3 pain, 1 other neurologic, 2 skin, 1 local, 2 fever w/o infection, 5 malaise/fatigue, 2 hyperglycemia, 2 hypoglycemia, 1 hyponatremia, 1 other metabolic, 2 fibrinogen, 3 prothrombin time, and 3 partial thromboplas. Grade V toxicities include 9 infection, 1 ARDS, 9 other pulmonary, and 1 ischemia.

This study was closed to enrollment effective November 10, 1995, due to increased incidence of treatment-related deaths and second malignancy reported in one arm of the study (none at WRAMC).

Adverse event memos sent to DCI on 4/18/96 and 4/22/96.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.



## DETAIL SUMMARY SHEET

TITLE: CALGB 9581 Phase III Randomized Study of Adjuvant Immunotherapy with Monoclonal Antibody 17-LA vs. No Adjuvant Therapy Following Resection for Stage II (Modified Astler-Coller B2) Adenocarcinoma of the Colon

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 28 October 1997

### STUDY OBJECTIVE

1) To determine whether adjuvant treatment with MoAb 17-1A will improve the probability of overall and disease-free survival, and increase disease-free intervals in patients who have undergone resection of a stage II colon cancer. 2) To evaluate a panel of prognostic markers, in order to correlate these measures with survival and disease recurrence in these patients.

### TECHNICAL APPROACH

Eligible patients with colon cancer will be randomly assigned after surgery to receive either adjuvant treatment with MoAb 17-1A, or standard treatment-observation. Patients receiving adjuvant therapy will receive doses of study IV over 2 hrs in the outpatient clinic, every 4 wks for a total of 5 doses. Treated group will have weekly clinic evaluations during treatment. Both groups will be followed q 6 months for 5 yrs.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this study or any study with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 4. The total number enrolled study-wide is 1656, if multi-site study. Grade 4 toxicities include 1 lymphocytes, 1 vomiting, 6 diarrhea, 1 other GI, 1 transaminase, 1 dyspnea, 1 dysrhythmias, 1 other heart, 3 allergy, and 1 malaise/fatigue. This study closed to enrollment effective 31 May 2002. Antibody supply for this trial will expire in late August. Therefore, in order to ensure that all patients enrolled will be able to complete their therapy by that time.

Ref: June 02 CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9581 – Phase III Randomized Study of Adjuvant Immunotherapy with Monoclonal Antibody 17-LA vs. No Adjuvant Therapy Following Resection for Stage II (Modified Astler-Coller B2) Adenocarcinoma of the Colon

KEYWORDS:

PRINCIPAL INVESTIGATOR: Joseph P. Drabick COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 28 October 1997  
New Anniversary Month: September

STUDY OBJECTIVE

1) To determine whether adjuvant treatment with MoAb 17-1A will improve the probability of overall and disease-free survival, and increase disease-free intervals in patients who have undergone resection of a stage II colon cancer. 2) To evaluate a panel of prognostic markers, in order to correlate these measures with survival and disease recurrence in these patients.

TECHNICAL APPROACH

Eligible patients with colon cancer will be randomly assigned after surgery to receive either adjuvant treatment with MoAb 17-1A, or standard treatment-observation. Patients receiving adjuvant therapy will receive doses of study IV over 2hrs in the outpatient clinic, every 4 wks for a total of 5 doses. Treated group will have weekly clinic evaluations during treatment. Both groups will be followed q 6 months for 5 yrs.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 4. The total number enrolled study-wide is 1656, if multi-site study. Grade 4 toxicities include 1 lymphocytes, 1 vomiting, 6 diarrhea, 1 other GI, 1 transaminase, 1 dyspnea, 1 dysrhythmia, 1 other heart, 3 allergy, and 1 malaise/fatigue. Adverse event reported January 22, 2003. This study closed to enrollment effective May 31, 2002.

Ref: CALGB Statistical Report

CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: Hemapheresis for Collection of Platelets for In Vitro Study of Platelet Cryopreservation

KEYWORDS: platelets, apheresis, storage, freezing, platelet induced clot retraction, thromboelastograph, protein phosphorylation, dynein, kinesin, nitric oxide, permeability coefficient, membrane phase transition, DMSO, blood storage bags – physical and thermal properties, dynamic mechanical analysis, glass transition temperature

PRINCIPAL INVESTIGATOR: Reid, Thomas COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: C  
INITIAL APPROVAL DATE: 24 June 1997

### STUDY OBJECTIVE

To study the effects of storage (freezing, 4°C, 20-24°C) on *in vitro* platelet function. To study the intracellular mechanisms (e.g. contractile proteins, membrane integrity, activation) of damage during storage. To study the biochemical mechanism of platelet induced clot retraction (PICR) and platelet activation.

### TECHNICAL APPROACH

Fresh platelets are stored at 22°C for five days and tested for *in vitro* platelet function, emphasizing PICR. Fresh, stored, or processed platelets and “platelet substitutes” are compared using *in vitro* function testing. Phosphorylated proteins identified with PAGE with 32P or MoAb against serine-P. Post translational modifications are identified using MoAb directed against modification. Using NO donors and various platelet agonists, platelets are tested for their ability to induce clot retraction and effect [Ca]<sub>i</sub> and [cGMP]<sub>i</sub>. Platelets are incubated with fluorescein diacetate. Platelets damaged during storage with a loss of membrane integrity can be identified by the release of fluorescein. The phase transition (T<sub>m</sub> liquid crystalline → gel) is evaluated using Fourier transform infrared spectroscopy (FTIR), nuclear magnetic resonance (NMR), differential scanning calorimetry (DSC), and electron paramagnetic resonance (EPR).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

One hundred six potential donors have been screened. Five were considered ineligible for donation, none in the past year. Forty-five participants have withdrawn from the study since its inception due to leaving the area. Seventeen individuals are available and eligible for apheresis (25%). Two hundred three apheresis procedures have been performed. All but two were successful (99 %). None were unsuccessful in the past year. Platelet membrane integrity is damaged on cooling or freezing without cryoprotectants. The platelet T<sub>m</sub> is approximately 15-18°C; DMSO appears to increase the T<sub>m</sub>. Model membrane studies are in the preliminary stages. To date, there has been no direct benefit to patients. The glass transition temperature and tensile module of several blood storage bags were studied.

The number of subjects enrolled to the study since the last APR at WRAMC is 0 and the total enrolled to date 99.

### CONCLUSIONS

Polyolefin bags appear ideal.

## DETAIL SUMMARY SHEET

TITLE: Chemoprevention of Prostate Cancer with Finasteride (Proscar) vs. Placebo

KEYWORDS: prostate cancer, finasteride, prevention

PRINCIPAL INVESTIGATOR: Schenkman, Noah LTC MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 30 November 1993

### STUDY OBJECTIVE

To determine if the medication "finasteride" can prevent prostate cancer. The effect of this treatment on the quality-of-life of the participants will also be determined.

### TECHNICAL APPROACH

A total of 40-60 men aged 55 or greater who are in good health will be enrolled in the study over one to two years. The digital rectal exam (DRE) must be normal, and the prostate specific antigen (PSA) must be three or less for all participants. There will be an annual visit, a 6-month visit and two phone contacts each year for seven years. At the annual blood visit a blood sample will be taken for PSA determination and a physical exam including DRE will be done. A six-month supply of placebo or finasteride will be dispensed. Quality-of-life information will be obtained at each contact.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The study stopped accrual on 6 December 1996. Sixty-three men were randomized to the clinical trial at WRAMC. Since the beginning of the study, three have transferred in and five transferred out. Five have withdrawn consent. Two subjects have died, one of pancreatic cancer and one during vascular surgery. Five have developed prostate cancer, two of those were found at the end-of-study prostate biopsy. The last patient to develop prostate cancer was active on study drug for only 6 months at the beginning of the study. He elected surgery and has been treated. Thirty-five of the 55 men have completed the seven-year study. The remaining 20 men will complete the study over the next two years. No patients withdrew from the study in the past year. There were no serious adverse events caused by the study drug here at Walter Reed or at other centers during the last year. Addendum 11, which allowed follow-up of each man after the 7 years is completed, was approved. To date no one has enrolled in this sub-study. Most of the men have elected to enroll in SELECT, the follow-on study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 63. The total number enrolled study-wide is 18,882. There will be no literature published until the end of the trial.

### CONCLUSIONS

There have been no conclusions to date.

## DETAIL SUMMARY SHEET

TITLE: Development of New Leishmania Diagnostic and Prognostic Indicators

KEYWORDS: leishmaniasis, nitric oxide, PCR

PRINCIPAL INVESTIGATOR: Aronson, Naomi COL MC

ASSOCIATES: Wortmann, Glenn LTC MC, Weina, Peter LTC MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Infectious Disease

INITIAL APPROVAL DATE: 26 May 1998

### STUDY OBJECTIVE

Obtain patient samples to identify new diagnostic and prognostic indicators for leishmania diagnosis.

### TECHNICAL APPROACH

Patient with suspected leishmaniasis and normal controls will be followed prospectively and have blood drawn before therapy (or day 0 for controls) and at days 7, 14 and 20 at 6-8 weeks. Urine will be collected for days 0-7 for measurement of nitrates. Skin biopsies from suspected patients will be used for PCR, leishmania culture and histopathology. Serum is obtained for measurement of soluble exoantigen and nitrates.

### PRIOR AND CURRENT PROGRESS

The number of subjects enrolled to the study since last APR at WRAMC is 6 and the total enrolled to date at WRAMC is 29. Interim literature review does not suggest any new information that would impact on this study. To date, twenty-one cases and eight controls have enrolled. Two controls were terminated for non-adherence to protocol requirements. There have been no adverse events identified. A change in two collaborating investigators was made due to retirement of prior collaborators.

### CONCLUSIONS

No results are available to date. Serum and urine samples are being collected to be run in aggregate.

## DETAIL SUMMARY SHEET

TITLE: Evaluation of the Clinical Efficacy of Antiretroviral Resistance Testing (CERT)

KEYWORDS: HIV, antiretroviral resistance

PRINCIPAL INVESTIGATOR: Aronson, Naomi COL MC

ASSOCIATES: Wortmann, Glenn LTC MC; Hawkes, Clifton LTC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Infectious Disease

INITIAL APPROVAL DATE: 07 July 1998

### STUDY OBJECTIVE

To determine the impact of genotypic and phenotypic antiretroviral resistance on the effectiveness of clinical care of HIV-1 infected subjects. To determine the feasibility of GeneChip HIV PRT assay and Antivirogram assays within clinical practice.

### TECHNICAL APPROACH

Local HIV patients are randomized to receive monitoring with genotypic, phenotypic (Antivirogram assay) or control (Roche Amplicor ultra sensitive PCR) viral load testing. All patients receive their viral loads at 4-month intervals. Those randomized to phenotypic or genotypic resistance testing arms, which have detectable viral loads > 1000 viral copies/ml will also have resistance testing done. Clinical changes in medications and the clinician use or non-use of the results of resistance testing to guide changes is information collected. An addendum (March 99) allows Virco therapeutic drug level monitoring for HIV drug levels in previously enrolled patients. An addendum (May 01) permits P450 polymorphism testing of cohort who enrolled and were taking the antiretroviral efavirenz.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

As of 15 May 2002, all patients have been terminated and the data analysis is in final review after a year of revisions. 455 persons total (with 80 at WRAMC) were enrolled in this long-term study to evaluate the clinical efficacy of resistance testing. At the WRAMC site there were 14 serious adverse events, one death due to homicide, and 13 hospitalizations. No SAEs were assessed as related to this protocol.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 80. The total number enrolled study-wide is 455, if multi-site study.

### CONCLUSIONS

There were no differences in demography between study arms at baseline. Median time of follow-up was 525 days. Median times to endpoint were 478 days, 521 days, and 574 days for the no-resistance testing, phenotypic, and genotypic arms, respectively. A KM analysis of time to endpoint stratifying by study arm and CDC stage showed a delayed time to endpoint for the resistance testing arms as compared to viral load only arm (Log rank  $p=.00035$ ) at 600 days of follow-up. There was no difference between the phenotypic and genotypic arms.

## DETAIL SUMMARY SHEET

TITLE: Cytokine Expression in Leishmaniasis Patients Treated with Sodium Stibogluconate (Pentostam) Therapy

KEYWORDS: leishmaniasis, Pentostam, cytokines

PRINCIPAL INVESTIGATOR: Aronson, Naomi COL MC

ASSOCIATES: Wortmann, Glenn LTC MC, Ockenhouse, Chris LTC MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Infectious Disease

INITIAL APPROVAL DATE: 30 November 1993

### STUDY OBJECTIVE

To describe and characterize cytokine expression of patients infected with *Leishmania* when receiving sodium stibogluconate or amphotericin. Based on cytokine expression, host immune responses will be classified as T-helper 1 or T-helper type CD4 subsets. Change in TH1 and TH2 responses will be described during therapy for insight into disease pathogenesis and therapy. Specific cytokine measurements will be performed and correlated to onset of pancreatitis.

### TECHNICAL APPROACH

Patients will be followed prospectively and have blood drawn before therapy and at days 7, 14, and 20 during therapy and at 6 weeks post-treatment. Serum is obtained for measurement of soluble CD4, IL-1B and TNF- $\alpha$ . Peripheral blood mononuclear cells will be obtained for RNA isolation and cell culture with phorbol ester stimulation. Enzyme immunoassay for specific cytokine measurement will be performed on serum and supernatant of cell cultures. Specific cytokine expression will be detected by reverse transcriptase polymerase chain reaction using specific cytokine primers. Addenda 8/99 to change assays to ELISPOT and ELISA for gamma interferon, IL4, IL 10, IL 12 and use *Leishmania* specific stimulation with various antigens and a control of Pentostam. Addenda 6/00 to allow *Leishmania* TAQman PCR of forty samples of banked PBMC pretreatment and, if positive, at subsequent collection time points. Addenda 2/02 allowed for up to twenty pre- and post-PBMC samples to be studied using an Affymetrix gene chip to assess immune responses elicited through profiling of signature patterns of gene expression.

### PRIOR AND CURRENT PROGRESS

Recent medical literature was surveyed using a Pubmed search engine. We have enrolled 45 cases and 10 controls. Enrollment has been stopped due to meeting target number. There have been no withdrawals. There are no reported adverse events. There is one protocol deviation. One amendment was submitted and approved since last APR. This allows for the study of twenty subjects using pre- and post-PBMC with the Affymetrix gene chip to assess immune responses during treatment. This is a laboratory study and there is no direct benefit for the participants. Serologic cytokine measurements on collected samples have been done. The white blood cells (PBMC) were found to be nonviable and this mitigated against doing many of the assays proposed. The *Leishmania* TAQman PCR of PBMC on forty patients were all negative. Data analysis of the results obtained from cytokine assays is ongoing. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 55.

### CONCLUSIONS

Pentostam produced elevations in the pancreatic enzymes during treatment of Leishmaniasis and this does not seem to be clearly related to measured cytokine expression. TH2 associated cytokines were negatively associated with early measures of amylase and lipase. Transient increases in nitric oxide with treatment correlated with a successful outcome. TAQman PCR for *Leishmania* was negative using PBMC from forty patients.

## DETAIL SUMMARY SHEET

TITLE: The Long-Term Efficacy of BCG Vaccine - A 56-Year Follow-Up

KEYWORDS: BCG, vaccine, tuberculosis

PRINCIPAL INVESTIGATOR: Aronson, Naomi COL MC

ASSOCIATES: Santosham, Mathuram MD; Harrison, Lee MD, Dana Mazo, Lewellys Barker MD, Lawrence Geiter DrPH

DEPARTMENT: Medicine

STATUS: O

SERVICE: Infectious Disease

INITIAL APPROVAL DATE: 05 December 1995

### STUDY OBJECTIVE

The primary objective of this study is to determine the duration of BCG vaccine efficacy in a Native American placebo-controlled trial with vaccination in the time period 1935-1942. Other related objectives are to describe the chronic disease morbidity and mortality, and to assess risk of malignancy in this group. Addendum 2/02 to allow for study in those who got TB...was there a difference BCG vs. Placebo in the severity of the TB using already collected information.

### TECHNICAL APPROACH

A total of 3,287 study participants are located, and Indian Health Service medical records reviewed. Death certificates are requested for all deceased. State tuberculosis and cancer registries are reviewed. Interviews are done for medical history for those without reviewed medical records.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No withdrawals. No serious or unexpected adverse events. Data collection is completed. Literature review shows that the study remains a unique observation. Statistical analysis continues and a manuscript has been completed. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 3,287. The total number enrolled study-wide is n/a if multi-site study.

### CONCLUSIONS

The incidence of TB was 66 and 138 cases per 100,000 person years in the BCG and placebo arms, respectively, for a vaccine efficacy since 1948 of 52% (95 CI: 27-69%,  $p=.0003$ ). Adjusting for age at vaccination, tribe, receipt of booster BCG, chronic medical illness, subsequent INH use, and BCG strain had little effect on the risk of TB. There was a trend of greater waning of effect in males as compared to females.



## DETAIL SUMMARY SHEET

TITLE: Sodium Stibugluconate (Pentostam) Pharmacokinetics Protocol

KEYWORDS: pharmacokinetics, Pentostam, leishmaniasis

PRINCIPAL INVESTIGATOR: Aronson, Naomi COL MC

ASSOCIATES: Wortmann, Glenn LTC MC

DEPARTMENT: Medicine

SERVICE: Infectious Disease

STATUS: C

INITIAL APPROVAL DATE: 11 June 1997

### STUDY OBJECTIVE:

To provide therapy with the drug Sodium stibugluconate (Pentostam) to patients with the confirmed diagnosis of leishmaniasis. To obtain pharmacokinetic data for patients varying in weight to provide information about the safety and appropriateness of daily dosing of sodium stibugluconate (Pentostam) at 20 mg/kg/d. A sub-objective will be to assess if daily dosing should be on the total or lean body weight.

### TECHNICAL APPROACH:

Blood and urine samples are obtained before, during and after pentostam (sodium stibugluconate) therapy as specified in the protocol. Serum and urine antimony levels are determined by two assays at Ft. Detrick and Yale University. No modifications or addenda to protocol have occurred.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE:

Nine patients have been enrolled at WRAMC. There have been no withdrawals; all nine completed the protocol. One adverse event occurred during the entire protocol, and was a vaso-vagal episode in one volunteer post blood draw. Serum and urine antimony levels have been assayed. Pharmacokinetic modeling has been completed. Clinical correlation of toxicity and efficacy information is being correlated with the antimony levels. A draft manuscript is in progress. Data from other sites is not available to the PI. Literature review shows no new studies on similar information. There is no benefit to participants.

The number of subjects enrolled to the study since the last APR at WRAMC is 0, and the total enrolled to date at WRAMC is 9. The total number enrolled study-wide is not known, if multi-site study.

### CONCLUSIONS:

Pharmokinetic modeling has been completed. The WRAMC participants in this CDC directed study provided information up to 16 hours after infusion that is a unique observation. In addition, we were able to provide detailed information from our frequent monitoring for toxicity that will be unique to our site (e.g. pancreatic enzymes and clinical pancreatitis). Data from this study may lead to changes in recommendations as to best dosing and treatment regimens with sodium Stibogluconate, the drug of choice for many forms of leishmaniasis.

## DETAIL SUMMARY SHEET

TITLE: Alteration in Colonic Motility Secondary to Inflammatory Bowel Disease

KEYWORDS: radiotherapy, prostate cancer

PRINCIPAL INVESTIGATOR: Whiteman, Sunny CPT MC

ASSOCIATES: Terez Shea-Donohue, Ph.D., Steve Lawson CPT MC, Christopher Swiecki, MD, Scott Rehrig, MD, Aiping Zhao, MD, Sherry Fleming, Ph.D., Daniel Otchy, MD

DEPARTMENT: Surgery

STATUS: C

SERVICE: General Surgery

INITIAL APPROVAL DATE: 20 April 1999

### STUDY OBJECTIVE

To examine the neuronal control of smooth muscle and mucosal function in inflammatory bowel disease through the *in vitro* changes and the contribution of nitric oxide.

### TECHNICAL APPROACH

There have been no new modifications. Contractions were assessed in mucosa-free muscle strips from human colon (UC, n=5, control, n=5) suspended in organ baths. Responses to acetylcholine (ACH) and nerve stimulation (EFS) were measured in the presence and absence of nitric oxide synthase inhibitor (L-NNA) or the  $\alpha$  and  $\beta$  adrenergic antagonists, phentolamine and propranolol (P + P). Mucosal permeability and epithelial cell secretion was measured by mounting muscle-free segments of bowel on an Ussing chamber to access short circuit current. The role of nerves was assessed by comparing responses to ACH and substance P (SP) in the presence and absence of TTX.

### PRIOR AND CURRENT PROGRESS

Ulcerative colitis (UC) is a chronic inflammatory disease characterized by severe diarrhea. Extrinsic and intrinsic nerves control colonic function. Ablation of sympathetic nerves (extrinsic) reduces inflammation in models of UC. The role of enteric (intrinsic) nerves in the altered smooth muscle and mucosal function in UC patients is unknown.

As previously reported in the last addendum, we have shown that, when compared to tissue taken from healthy controls undergoing resection of colon for cancer or adenoma, smooth muscle obtained from surgical resection of patients with ulcerative colitis exhibit an increase in the frequency of spontaneously occurring contractions. In addition, the muscle also shows a decreased responsiveness to nerve stimulation and to the neurotransmitter acetylcholine. This latter effect can be attributed in part to an up-regulation of inhibitory sympathetic neural input to the colon. In patients with ulcerative colitis, there is an increased permeability of the epithelium and markedly reduced secretion in response to neurotransmitters substance P and acetylcholine.

There has been no progress since the last addendum was submitted. From the review of this protocol, seven enrolled patients' consent forms could be located, which were submitted to DCI. The remainder of the previously recruited patients' consent forms was unable to be located and thus have not been able to be used as part to the study. No new patients were enrolled. There have been no adverse events. We are requesting that this study be discontinued.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 7. The total number enrolled study-wide is N/A, if multi-site study.

### CONCLUSIONS

We conclude that increases in frequency of contractions and mucosal permeability and inhibition of intrinsic neural control of colon smooth muscle and mucosal function contribute to the severe diarrhea in UC. Upregulation of the "sympathetic brake" in UC acts to slow colonic motility in an effort to compensate for the loss of control by intrinsic nerves. These effects may be central to the maintenance of abnormal motility in inflammatory bowel disease.

## DETAIL SUMMARY SHEET

**TITLE:** Does Protease Gene Expression Vary by Location in the Lower Extremity in Patients with Primary Varicose Veins or Chronic Venous Insufficiency as Compared to Controls?

**KEYWORDS:** MMP, varicose veins

**PRINCIPAL INVESTIGATOR:** Gillespie, David LTC MC  
**ASSOCIATES:**

**DEPARTMENT:** Surgery  
**SERVICE:** Peripheral Vascular Surgery

**STATUS:** O  
**INITIAL APPROVAL DATE:** 2 February 1999

### STUDY OBJECTIVE

1. Compare the expression of MMP-1, MMP-3, MMP-7, MMP-13, and tryptase in varicose veins as compared to non-varicose veins.
2. To quantify and localize these protein levels comparing the upper thigh vein to lower leg vein.
3. To compare their enzymatic activity

### TECHNICAL APPROACH

In this study, segments of greater saphenous vein are obtained from patients undergoing CABG or varicose vein surgery. These veins are processed and both total RNA and total protein isolated. The RNA is then reverse transcribed using the First Strand cDNA Synthesis Kit (Boehringer Mannheim, Indianapolis, IN) using primers specific for MMP-1, 3, 7, 13, and tryptase. RT-PCR product is then separated over 2% agarose gel containing ethidium bromide (0.5 &g/&ml) and visualized by UV irradiation and will be photographed using a Polaroid documentation system.

Western blots are performed using monoclonal mouse anti-human antibodies MMP-1, MMP-3, MMP-7, MMP-13, and tryptase as the primary antibodies (Oncogene Science, Cambridge, MA). Goat antimouse horseradish peroxidase coupled antibodies will be used as secondary antibodies. Scanning densitometry is then performed (NIH imager v.1.57) to quantify the amount of these proteins in each sample. Activity of these enzymes is then analyzed.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

We are currently working under an amendment to the original protocol. In this amendment we were approved to perform RT-PCR, Western Blot analysis and zymography for MMP-1, 3, 8,13, and tryptase, on 15 additional control patients. Prior to taking specimens of their greater saphenous vein we plan to obtain a preoperative air plethysmography (APG) on the patient's leg that is to be used for vein harvest.

The number of subjects enrolled to the study since last APR at WRAMC is 5 and the total enrolled to date at WRAMC is 27. The total number enrolled study-wide is 27, if multi-site study.

### CONCLUSIONS

We are in the process of completing the RT-PCR, and Western Blot analysis for MMP-1, 3, 8,13, and tryptase, on 15 additional control patients.

## DETAIL SUMMARY SHEET

TITLE: Initial Evaluation of Excimer Laser Keratorefractive Surgery in US Army Personnel

KEYWORDS: Refractive surgery, laser, excimer laser, lamellar, photorefractive keratectomy, contrast

PRINCIPAL INVESTIGATOR: LTC Kraig Bower MC

ASSOCIATES: LTC Jeff Rabin MC, MAJ Prem Subramanian MC, MAJ Robert Bauer MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: Ophthalmology

INITIAL APPROVAL DATE: 20 April 1999

### STUDY OBJECTIVE

The objective of this study is to conduct a prospective clinical trial to evaluate the safety and efficacy of the VISX Excimer Laser System for the treatment of naturally occurring low to moderate myopia, with or without low levels of astigmatism, in U.S. Army personnel.

### TECHNICAL APPROACH

Master protocol modifications approved. Separate sub-protocols approved:

- a. Night Vision Goggle and Night Firing Range Performance After Myopic Excimer Laser Keratorefractive Surgery in U.S. Army Personnel
- b. Prospective Evaluation of Keratorefractive Surgery in Army Aviator Trainee
- c. Operational Assessment of Refractive Surgery for Rated Army Aviators: A Prospective Evaluation

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are three DCI-approved sub-protocols under this Master Protocol. APRs are reported separately. Briefly, there are 19 patients treated under the Master protocol. Their results are being evaluated in detail. No adverse events are noted in that group. Under the NVG sub-protocol (WU # 01-2335-99a), we have treated a total of 20 patients with no adverse events. Most have been followed through their 3-month postop visits. Enrollment of the remaining subjects as well as the control group is delayed due to unavailability of soldiers as they deploy or prepare to deploy for the war effort. We have not yet enrolled any subjects under the Aviator trainee sub-protocol (WU # 01-2335-99b); we are making final revisions required by HSRRB and then final written approval before we proceed as planned. Under the Rated aviator sub-protocol (WU # 01-2335-99c), we have enrolled and treated a total of 14 patients. There have been no adverse events from that sub-protocol. Consideration is under way to submit a modification of that sub-protocol to allow us to drop the PRK arm of the study and proceed only with LASIK subjects. The justification for considering this option is covered under separate APR.

The number of subjects enrolled to the study since last APR at WRAMC is 34 and the total enrolled to date at WRAMC is 53. The total number enrolled study-wide is N/A, if multi-site study.

### CONCLUSIONS

We will continue to enroll subjects under the NVG sub-protocol once they are available to comply with the treatment and follow-up schedule as specified in the protocol. We are working on finalizing the HSRRB-required revisions to the Aviator trainee sub-protocol. We will seek guidance from DCI on modification of the Rated aviator sub-protocol.

## DETAIL SUMMARY SHEET

TITLE: Auditory Processing and Sensorineural Hearing Loss

KEYWORDS: hearing loss, active mechanism

PRINCIPAL INVESTIGATOR: Summers, Van Ph.D, DAC

ASSOCIATES: Leek, Marjorie Ph.D, DAC

DEPARTMENT: Surgery

SERVICE: Army Audiology and Speech Center

STATUS: O

INITIAL APPROVAL DATE: 14 March 1997  
(Umbrella Study)

### STUDY OBJECTIVE

This work unit is a grant proposal; submitted to the National Institute of Health to obtain funding. The grant involves a physiological process in the inner ear referred to as the active mechanism. The research examines 1) a possible psychoacoustic means of evaluating active mechanism status in individual listeners and 2) the role of the active mechanism in improving signal detection and speech recognition in selected competing sounds.

### TECHNICAL APPROACH

Each of the proposed experiments involves auditory testing of normally hearing and hearing-impaired listeners. The basic task of the subjects is similar to procedures used clinically to evaluate hearing. Subjects listen to sounds (both speech and non speech) over earphones while seated in a sound-treated booth. They make responses indicating their detection or identification of these sounds by touching specific areas on a touch screen terminal.

### PRIOR AND CURRENT PROGRESS

Three experimental studies described in the NIH grant have been completed under individual work unit numbers. No patients have been or will be enrolled under this work unit number for these three experiments. An addendum to this work unit number was approved by the Human Use Committee on 20 June 2000 which allows the remaining experiments described in the NIH grant to be carried out under this work unit number (experiments 5-8 in the grant). A revised consent form appropriate to these experiments was approved at that time. We have now completed data collection for experiment 7 that examines how presentation level influences speech recognition performance in the presence of continuous and fluctuating background sounds. We have completed a manuscript describing the results that is presently being circulated for in-house reviews. The manuscript will be submitted for publication in February of 2003. The number of subjects enrolled under this work unit number since last APR at WRAMC is 21 and the total enrolled to date at WRAMC is 25.

### CONCLUSIONS

The results supported previous studies in indicating that normal-hearing listeners had much less difficulty in recognizing speech masked by a fluctuating background signal (either a single competing talker or the same competing signal played backwards) than by continuous noise with little amplitude modulation. For these listeners, the difference in performance between the fluctuating and continuous background conditions was level dependent: the performance difference was reduced at high presentation levels. This result is consistent with the idea that the cochlear active mechanism contributes to the difference in speech recognition performance for fluctuating vs. continuous maskers. The influence of the active mechanism is reduced with increases in presentation level that may partially account for similar performance across the two-masker types at high levels. Hearing-impaired listeners showed only small differences in performance for across masker types and presentation levels. These results may reflect the loss of active processing associated with the cochlear hearing loss.

## DETAIL SUMMARY SHEET

TITLE: Hearing Loss and the Perception of Complex Sounds

KEYWORDS: hearing impairment, frequency resolution, time perception

PRINCIPAL INVESTIGATOR: Leek, Marjorie PhD

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: O

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 26 August 1997

### STUDY OBJECTIVE

Patients with hearing loss have difficulty understanding speech in noise because of much functional impairment within the ear, including reductions in the ability to carry out precise spectral and temporal analyses of sound. Studies in this program of research explore these analytic abilities in hearing-impaired and in normal hearing people, with the ultimate goal of increasing the benefits derived by hearing-impaired patients through the use of hearing aids.

### TECHNICAL APPROACH

All of the experimental techniques used in these studies involve earphone presentation of sounds to a subject, who indicates his perception through the use of a touch-screen terminal. Experiments often require listeners to detect a low-intensity sound buried in noise or ask listeners to judge whether two sounds are the same or different. Acoustic stimuli are generated to test specific hypotheses concerning functional effects of hearing loss.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This is an NIH grant that contains a number of experiments. I requested and was granted a two-year extension of this work unit in August of 2002. During the past year, we have initiated data collection on one additional experiment that measures discrimination of glides in both frequency and amplitude by normal-hearing and hearing-impaired subjects.

The number of subjects enrolled to the study since last APR at WRAMC is 9 and the total enrolled to date at WRAMC is 52. There have been no adverse reactions and no patients have withdrawn from these studies. There is no direct benefit to patients who participate in this study.

### CONCLUSIONS

Preliminary results of the glide study indicate that glides sweeping upwards in frequency support better discrimination when their amplitudes are decreasing rather than increasing. There appear to be no differences due to amplitude contour in glide discrimination for downward frequency sweeps. Discrimination is poorer for all stimuli in the frequency region of 3200 Hz, relative to performance at frequencies near 1600 Hz. These results suggest that dynamic changes in amplitude and frequency, such as are found in speech sounds, are discriminated differently for upward and downward sweeps, and these differences might be related to shifts of the peak of the traveling wave on the basilar membrane. These conclusions should be viewed with caution, as data collection is still ongoing.

## DETAIL SUMMARY SHEET

TITLE: Complex Sound Analysis by Persons with Impaired Hearing (Application for NIH NRSA Post Doctoral Fellowship)

KEYWORDS: hearing loss, complex sounds, sound segregation

PRINCIPAL INVESTIGATOR: Leek, Marjorie, PhD DAC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: O

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 14 September 1999

### STUDY OBJECTIVE

The perception of specific sounds in a complex background of sounds is an important aspect to communication. Often times we communicate in the midst of a rich acoustic environment in which many sounds are present with vastly different temporal and spectral characteristics. It is well-known that a healthy auditory system has the ability to distinguish different sound sources from one another and attend to a particular sound source amid multiple sound sources, but less is known regarding the abilities of a damaged auditory system to make use of the prevalent cues in a complex acoustic scene. The main goal of this research protocol is to assess the abilities of hearing-impaired listeners to segregate sounds in a 2-source environment and compare their abilities with those of normal-hearing listeners. We will assess whether the damage to the cochleas in hearing-impaired listeners limits their ability to distinguish one sound from another using certain cues.

### TECHNICAL APPROACH

Listeners will hear four short, multi-tonal stimuli presented over headphones. The first two sounds will be played simultaneously. Next, the two sounds will be played again, but one of those sounds will have different spectral characteristics. The listener is asked to indicate on a touch-screen terminal which sound (the third sound or the fourth sound) was changed. Depending on the characteristics of the sounds, listeners will hear the first two simultaneously-presented sounds as either one sound or two sounds. If the listeners hear the two sounds as if they were one, the task will be extremely difficult to do. However, if the listeners hear the two sounds separately, they will easily distinguish which sound changes across the presentations. Different aspects of the sounds will be changed to evaluate when the two sounds are heard as a single sound or heard as two sounds. In some experiments, the onset times of the two sounds will be varied. Sensitivity will be measured as a function of onset time difference. In other experiments, the sounds will be modulated at different rates, and sensitivity will be measured as a function of modulation rate difference.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

We have now completed data collection on the onset asynchrony portion of this study. This part measures the ability of hearing-impaired listeners to use differences in the onset of different spectral regions of complex sounds in order to better hear those frequencies. We have initiated data analysis on this study. The number of subjects enrolled to the study since last APR at WRAMC is 7 and the total enrolled to date at WRAMC is 11. There have been no adverse reactions and no subjects have withdrawn from the study. There is no benefit to the subject.

### CONCLUSIONS

Onset differences within a complex sound do not assist hearing-impaired listeners to hear out certain frequency regions when the sound bandwidth is narrow. However, for wide bandwidth sounds, there is a small advantage for onset differences less than about 50-100 ms between frequency regions. The advantage, however, is too small to suggest a practical application to assist speech understanding by altering the onset relationships among frequency regions.

## DETAIL SUMMARY SHEET

TITLE: Monitoring for Donor-Specific Hyporesponsiveness Following Renal and Pancreatic Allotransplantation

KEYWORDS: Kidney Transplant

PRINCIPAL INVESTIGATOR: Allen Kirk, M.D. Ph.D., NIDDK

ASSOCIATES: S. John Swanson, COL, MC

DEPARTMENT: Surgery

SERVICE: Organ Transplant

STATUS: O

INITIAL APPROVAL DATE: 22 June 1999

### STUDY OBJECTIVE:

Primary Protocol Objective:

The primary objective of this protocol is to develop methods of evaluating patients after transplantation that detect donor-specific immune hypo-responsiveness or tolerance.

Secondary protocol objectives include:

1. To monitor patients clinically and generate base-line data on donor specific immune responses that occur following transplantation with conventional immunosuppression. These observations will be used as a comparison for future trials using novel immunomodulatory regimens.
2. To correlate long-term patients and graft outcome with findings from the techniques developed. While this study is not powered to clinically correlate these techniques, it is hoped that pilot data can be obtained during assay development indicating that immune hypo-responsiveness to donor antigen results in improved graft survival. Formal study of this will involve subsequent protocol development.

### TECHNICAL APPROACH:

An unlimited number of transplant patients will be enrolled. In addition, up to 20 normal, non-uremic volunteers will be enrolled to establish a normal baseline for peripheral blood assays. Samples received from transplant patients prior to transplant will serve as uremic controls.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE:

Open to accrual. The number of subjects enrolled to the study since last APR is 0. Total enrolled to date at WRAMC is 0. A total of 187 patients have been enrolled in this protocol, 19 since last Continuing Review. Of the patients enrolled to date, 106 are healthy volunteers, 23 are long-term post transplant patients transplanted elsewhere. 57 are patients who proceeded to renal transplantation at the clinical center. One-year graft survival remains at 100% for patients transplanted on this protocol at the clinical center. Two grafts have been lost after the first year (one kidney and one pancreas) secondary to rejection.

This study has provided the Transplantation and Autoimmunity Branch of NIDDK and Army investigators with important information on the natural history of allotransplant function, immune function, and intragraft histology under the standard of care, and, as such, has served as a reference point for contemporaneous investigational agent protocols. This trial has also provided tissue allowing the investigators to develop a novel real-time polymerase chain reaction assay for characterization of the transcriptional events occurring as a result of allograft reperfusion and immune attack. This assay has served as the topic of a Cooperative research and Development Agreement (CRADA) with Applied Biosystems. Additional information has been obtained through the analysis of cytokine gene polymorphisms. Correlates between outcome and polymorphism have aided to the design of investigational protocols. This protocol has also been used to evaluate the transcriptional profile of reperfusion injury. NIDDK investigators outside of the Transplantation and Autoimmunity Branch have enrolled these patients in multiple renal pathophysiology trials, thus this protocol has provided NIH with a patient population (renal transplant recipients) unavailable elsewhere in the clinical center.



#### Work Unit # 2635-99 [Continued]

There have been 14 Serious Adverse Events reported since the last CR as noted below.

- Bilateral avascular necrosis of the hips – left femur fracture
- Wound infection following orthopedic procedure
- Elevated blood sugars
- Urinary tract infection
- Human papillomavirus associated with genital warts
- Fever of unknown origin
- Hernia repair
- Bowel obstruction
- Death
- Transitional cell carcinoma of the bladder
- Steroid resistant acute rejection
- Death
- Tertiary hyperparathyroidism
- Ventral hernia repair

There was one unexpected serious adverse event (4 December 2002 - transitional cell carcinoma of the bladder) during this reporting period. A 42-year-old white male who underwent a living unrelated donor renal transplant on 15 October 2002 did well postoperatively. Following removal of his urinary catheter he had difficulty completely emptying his bladder. He was taken to the operating room for cystoscopy and probable bladder neck incision. However, a pedunculated tumor was discovered at the bladder neck, and excised. Given the immediate onset of symptoms with voiding and the size of the polyp at exploration, it is likely that this lesion was present postoperatively, and is not the result of the operative procedure or immunosuppression. Rather, it is likely that re-establishment of renal function allowed for this lesion to be detected and excised early in its growth.

There have been four deaths associated with this protocol. Two deaths have occurred since the last CR. The first patient, a recipient of a kidney-pancreas allograft, died three years post transplant of a narcotics overdose. A toxicology screen at autopsy showed toxic levels of Oxycodone Hydrochloride, Mirtazapine, and Doxepin Hydrochloride. The coroner determined the death to be “accidental”. The second patient died secondary to congestive heart failure, pneumonia, and hemorrhage post bronchoscopy during an acute pulmonary episode. Both deaths occurred outside of the clinical center in patients with functioning allografts.

There have been no subject withdrawals during this CR period. Seventeen relevant publications and abstracts have resulted from this research. Two amendments were made to the protocol and standard consent form since the last CR.

We wish to report on a patient who completed their treatment course under the special exception protocol 01-DK-9970 An Open Label Comparative Protocol for the Emergency Use of Voriconazole (UK109,496) in Patients With Life-Threatening Invasive Mycoses Who Are Failing on Current Available Antifungal Agents during this CR period while participating in 99-DK-0119. The patient completed their course of Voriconazole without problems. The patient’s fungal infection clinically resolved. All study paperwork and safety reporting was completed and submitted to Pfizer Central Research who managed the trial.

#### CONCLUSIONS:

This protocol needs to be maintained to continue to provide biopsy and peripheral blood samples for transcriptional and polymorphism studies. It is also necessary to provide a reference point for graft outcome to which investigational therapies can be compared.

## DETAIL SUMMARY SHEET

TITLE: Live Donor Renal Donation for Allotransplantation

KEYWORDS: Kidney Donor

PRINCIPAL INVESTIGATOR: Allen Kirk, MD, PhD

ASSOCIATES: S. John Swanson, COL, MC

DEPARTMENT: Surgery

SERVICE: Organ Transplant

STATUS: O

INITIAL APPROVAL DATE: 22 June 1999

### STUDY OBJECTIVE:

This protocol is designed to identify candidates for renal donation and provide donor kidneys for patients undergoing renal transplantation as part of protocol related studies at the NIH Clinical Center. This protocol will also be used to facilitate the procurement of donor blood and bone marrow in support of transplant studies involving the evaluation of donor specific immune reactivity.

### TECHNICAL APPROACH:

The eligible population will be adults without preexisting renal disease who are willing to donate a kidney to a family member or close friend who is enrolled in a clinical transplant protocol at the NIH Clinical Center. Patients will be considered providing they are in good general health. While each patient is evaluated individually, symptomatic cardiac disease, cerebrovascular disease, or peripheral vascular disease will generally lead to the exclusion of the candidate. Also, most contagious infectious diseases contraindicate donation, although this is dependent in large part on the infectious status of the recipient. For example, an individual with Hepatitis C would not be acceptable for general donation but might be able to donate to another individual with the same strain of hepatitis C virus.

Patients will not be selected according to race and gender. However, because some of the disorders under study have different demographic characteristics, the patient populations will not be expected to be evenly balanced (e.g. refractory hypertension). By international convention, children are not allowed to be used as living organ donors regardless of whether their guardians consent. For this reason, only adults will be considered for donation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE:

Protocol is currently open to accrual. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. A total of 111 patients have been enrolled in this protocol study-wide – 28 since the last Continuing Review. Of the patients enrolled, twelve have proceeded to renal donation, and sixteen have been medically excluded. All patients remain alive and well with good renal function.

Patients accrued to this protocol have proceeded to donation have all done well post operatively. However, two patients have experienced Serious Adverse Events as described below. These events were reported at the time of their occurrence. All kidneys from this protocol have functioned well post transplantation. Eleven of twelve grafts transplanted during this enrollment period functioned immediately, while one graft had delayed function that was attributable to a correctable technical issue in the recipient. This was unrelated to the status of the donor graft. No kidney from this protocol has been lost to rejection or technical failure.

#1 – A 5-year-old white female underwent a donor nephrectomy for a protocol renal transplant recipient on 22 October 2002. Her procedure was technically unremarkable. Anti-thromboembolism prophylaxis was used as is our standard practice including systemic heparinization during the vascular manipulations of the procurement, application of sequential compression devices, and anti-embolism stockings from the pre-operative period until the patient was ambulating freely post operatively, and early post operative ambulation (<24 hours post op). Her peri-operative course was unremarkable. She returned home by plane one week following donation. On 2 November

2002, the patient experienced shortness of breath, and sudden left sided pain. She went to her local emergency room and was hospitalized for a presumed pulmonary embolus. A chest radiograph was reported to be suggestive for pulmonary embolus. No VQ scan was performed. Her local physician on clinical grounds made the diagnosis of a pulmonary embolus. The patient was stable throughout her course and was heparinized, converted to coumadin, and discharged to home.

Pulmonary embolism can occur following any major operative procedure. Its incidence is reduced by the use of anti-embolism prophylaxis, and in this case, all methods reported to be appropriate were employed. The risk of pulmonary embolism is specifically detailed in the protocol consent. Pulmonary embolism can also occur as a result of air travel or other sedentary activities.

#2 – A 38-year-old white male who underwent a donor nephrectomy for a protocol renal transplant performed on 18 June 2002. Both his peri-operative course and that of his recipient were unremarkable. The patient was admitted on 4 December 2002 for complaints of pain over his incision site. He reported that the pain began “about a month” prior and had worsened. He denied any fever or GI symptoms. A CT scan was performed at his local hospital showing a fluid collection in the operative bed and a possible foreign body. On admission to the NIH, a plain film of the abdomen revealed a retained operative sponge. On 5 December 2002, the patient underwent a surgical exploration. The patient was found to have a 4x8 sponge in the operative site associated with a sterile (by gram stain) reactive fluid collection. The patient was put on antibiotics until intraoperative cultures returned negative. The patient recovered well post operatively, remained afebrile after withdrawal of antibiotics, and was discharged to home on 11 December 2002.

This is clearly a technical error. Review of the operative record showed that the sponge and instrument counts were reported to the operative surgeon as correct at the time of closure. The operative team and the operating room staff have reviewed this incident, and a formal Occurrence Report has been generated. A root cause analysis performed on 14 February 2003 determined this to be caused by nursing error.

#### CONCLUSIONS

Living related and unrelated kidney donation provides over 50% of the organs for renal transplant protocols at the Clinical Center, and remains an invaluable source of organs for tolerance protocols. It also is an irreplaceable source of normal renal tissue and normal, uni-nephric individuals for the study of ischemia reperfusion injury and allo-independent aspects of renal transplantation. Living donation is preferred for experimental transplantation, as it eliminates many of the variables that confound transplant protocol interpretation.

## DETAIL SUMMARY SHEET

TITLE: Establishment of a Serum Bank for the Future Detection of New Prostate Cancer Markers in Serum of Patients with Prostate Cancer, Benign Prostate Conditions and No Prostate Disease

KEYWORDS: serum, prostate, future

PRINCIPAL INVESTIGATOR: COL J. Moul, MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: O  
INITIAL APPROVAL DATE: 6 December 1994

### STUDY OBJECTIVE

Primarily: to establish a serum bank. Serum will be obtained from patients with prostate cancer, benign prostate disorders and no prostate disease to use in the evaluation of new markers of disease.

### TECHNICAL APPROACH

Thirty ccs of blood will be drawn and spun down, and the serum will be frozen for use in the future.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no adverse events since the last APR. No patients have withdrawn from the study since the last APR. There are no new literature findings to report.

This study was granted an exception to policy 4 January 2002 for a one-year extension, through 31 December 2002. A new Master Serum Protocol has been submitted and is currently scheduled for the December 2002 CIC and the January HUC. Therefore, we are submitting along with this APR a request for exception to DCI policy to keep this protocol open until the new protocol is approved. On 22 March 2002 the PI for this protocol was changed. On 5 November approval was received for adding DeWitt as a site to this protocol.

The number of subjects enrolled to the study since last APR at WRAMC is 303 and the total enrolled to date at WRAMC is 2038. The total number enrolled study-wide is N/A, if multi-site study.

### CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: Medical Therapy in Benign Prostate Hyperplasia - Full-Scale Trial

KEYWORDS: prostate, medical therapy, BPH

PRINCIPAL INVESTIGATOR: Schenkman, Noah LTC MC

ASSOCIATES: David McLeod, Judd Moul, Robert Dean, Kevin Gancarczyk, Mark Gibbons, Greg Griewe, Edmund Paquette, Stephen Brassell, Burkhardt Zorn, Kimberly Peay, Maria Rueda, Thomas Esther, Rayford Petrowski, Stacy Koff, Inger Rossner

DEPARTMENT: Surgery

STATUS: C

SERVICE: Urology

INITIAL APPROVAL DATE: 31 January 1995

### STUDY OBJECTIVE

To determine the effectiveness of medical therapy (finasteride and/or doxazosin) to treat, delay or prevent the symptomatic progression of benign prostatic hyperplasia (BPH) and to assess differences over time between treatment groups. To investigate prognostic indicators and biologic parameters regarding response to therapy. To gain insight into biologic and physiologic natural history of prostate growth.

### TECHNICAL APPROACH

The study is multi-center, placebo-controlled, double-masked clinical trial in which patients who have been diagnosed with symptomatic BPH are randomly assigned to either of three drug treatment arms or a placebo control once all entrance criteria have been fulfilled. All patients are monitored closely and will undergo follow-up evaluation quarterly for efficacy, adverse events and overall mortality. The protocol was approved 5 May 1995 and addenda were approved 28 June 1995, 29 October 1996, 28 October 1997, 5 February 1998, 28 April 1998 and 20 July 2001.

### PRIOR AND CURRENT PROGRESS

Enrollment started December 1995 and ended January 1998. A total of 165 participants were randomized in the full-scale trial and 24 in the pilot study at WRAMC. Enrollment study wide was 3047. The following is a breakdown in status of the enrollees at WRAMC: Twenty-four participants were enrolled in the pilot study. There were two deaths, eight other inactives, four subjects off both medications, and four had progression of BPH. Five men crossed over to invasive therapy, and two developed prostate or bladder cancer during the entire study. One hundred sixty-five subjects were enrolled in the full-scale trial. There were six deaths, eight other inactives, nine progression of BPH, twenty-two developing prostate or bladder cancer, and sixteen crossing over to invasive therapy. Twenty-one patients were off both medications and seven were off one of the study medications. In the past year there have been no serious adverse events because the study was closed for data collection 30 November 2001. All patients were unblinded in June and July at their last study visit. They were given a copy of the conclusions of the study and graphs of their PSA, BPH Symptom Score results, and their Uroflow results over the seven-year course of the study. In addition, they were given printed information of the actual medications that the patient was taking while enrolled. All patients on study drug at the end of the study were given the option of remaining on study medication until their unblinding visits.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 189. 24 were on pilot study. 165 were on full-scale study. The total number enrolled study-wide is 3047.

### CONCLUSIONS

The study proved that the two drugs together are more effective for treating BPH than either alone. The results were presented at the American Urological Association (AUA) in Orlando on 28 May 2002. The Medical

Work Unit # 2804 [*Continued*]

Therapy of Prostatic Symptoms (MTOPS) Trial found that compared to placebo, the 5  $\alpha$ -reductase inhibitor finasteride and  $\alpha$ -1 receptor blocker doxazosin together reduced the risk of BPH progression by 67%. The risk of progression was reduced by 39% with doxazosin alone and by 34% with finasteride alone. Physicians at seventeen medical centers treated about 3000 men age 50 and up for an average of 4.5 years. The men all had BPH and were evenly divided into four groups that took either 5 mg finasteride, 4 mg or 8 mg doxazosin, both drugs, or a placebo. The aim of the trial was to prevent BPH progression, defined primarily as either a significant worsening of symptoms, recurring urinary tract infection, urinary retention, incontinence, or invasive therapy such as surgery. Compared to placebo, the risk of urinary retention was reduced by 79% with combination therapy, by 67% with finasteride, and by 31% with doxazosin (not significantly different from placebo). The risk of invasive therapy was reduced by 69%, with the combination by 64%, with finasteride by 8%, and with doxazosin no significant percent from placebo.

## DETAIL SUMMARY SHEET

TITLE: Multicenter Prospective Cohort Study to Evaluate the Safety and Effectiveness of the American Medical Systems (AMS) Ambicor™ Inflatable Penile Prostheses

KEYWORDS: Ambicor, implant, prostheses

PRINCIPAL INVESTIGATOR: McLeod, David COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: O  
INITIAL APPROVAL DATE: 29 August 1995

### STUDY OBJECTIVE

To evaluate the ability of the AMS penile prosthesis to provide an erection suitable for sexual intercourse (device function) as determined by PE and patients self report. Safety will be evaluated by measuring rates of complications and the occurrence of medical conditions associated with the device.

### TECHNICAL APPROACH

After patients have made a decision to have an Ambicor™ implant, they are informed about the study. Pre-study/screening lab work must be completed prior to surgery. After surgery, the patient cannot use the device for sexual intercourse for six weeks. Follow-up exams will be at 6 weeks, 6 months, 1 year, and 18 months post-implant. Patients will complete questionnaires at these visits. Complications, associated medical conditions, and other adverse effects will be followed for 18 months.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 19. The total number enrolled study-wide is 140, if multi-site study.

### CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: A Randomized, Double-Blind Comparative Trial of Bicalutamide (Casodex) vs. Placebo in Patients with Early Prostate Cancer

KEYWORDS: prostate cancer, Casodex

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

ASSOCIATES: Moul, Judd COL MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: Urology

INITIAL APPROVAL DATE: 28 November 1995

### STUDY OBJECTIVE

The primary objective is to compare 2 years of adjuvant bicalutamide 150 mg monotherapy with placebo in terms of clinical progression and overall survival. The secondary objectives are to compare 2 years of adjuvant bicalutamide 150 mg monotherapy with placebo in terms of time to treatment failure and tolerability and to investigate the association of serial measurement of serum PSA and treatment outcome following 2 years of adjuvant bicalutamide therapy vs. placebo.

### TECHNICAL APPROACH

This is a double blind, randomized clinical trial evaluating bicalutamide (Casodex) 150 mg monotherapy vs. placebo as adjuvant therapy with early prostate cancer.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Enrollment was completed in August of 1997. 3,292 patients were enrolled in this study nationwide. Twenty-four (24) patients were enrolled at WRAMC. We have received no new adverse reports from other sites. All serious unexpected adverse events from WRAMC have been reported. Twenty-two (22) patients have completed the active part of the study and are being followed for survival and disease progression per protocol. Five (5) patients have started on second line therapy as a result of disease progression. One (1) patient has voluntarily withdrawn from the study and is lost to follow-up and one (1) patient was lost due to death.

### CONCLUSIONS

Study is ongoing. No conclusions at this time.



## DETAIL SUMMARY SHEET

**TITLE:** A Phase II Study to Determine the Effects of Finasteride and Flutamide on Patients with Rising PSAs Who Have Had Radical Prostatectomy, Radiation or Cryoablation Treatment for Localized Primary Prostate Cancer

**KEYWORDS:** finasteride, flutamide, prostate

**PRINCIPAL INVESTIGATOR:** Moul, Judd COL MC

**ASSOCIATES:** McLeod, David COL MC

**DEPARTMENT:** Surgery

**SERVICE:** Urology

**STATUS:** O

**INITIAL APPROVAL DATE:** 27 February 1996

### STUDY OBJECTIVE

To determine in patients with Stage A, B, C, or D1 cancer of the prostate: 1) the likelihood of response in order to assess whether daily finasteride and daily flutamide should be advanced to other studies; 2) toxicity of daily finasteride with daily flutamide; and 3) the likelihood of potency maintenance in patients who were potent before the study.

### TECHNICAL APPROACH

Patients will receive flutamide and finasteride daily and will be followed for two years. If the patient remains responsive to the study drugs, they will remain on the lower dose and be followed for five years. If a patient has three consecutive rises in the PSA, the flutamide will be increased to full dose and the patient will be followed for survival data for five years.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Enrollment was completed in August 1997. All patients have completed the (2) two-year trial and are in the (5) five-year survival phase. Twelve (11) patients have continued to respond to low dose hormonal therapy, two (2) patients have advanced to full dose hormonal therapy, (8) patients have discontinued therapy due to inability to tolerate drug for expected side effects, twelve (14) patients have discontinued due to progression with rising PSA or other medically required issues, one (1) patient is lost to follow-up, and (3) patients died.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 39. The total number enrolled study-wide is 200, if multi-site study.

### CONCLUSIONS

Combination of flutamide and finasteride appears to be well tolerated and effective in short-term reduction of serum PSA for a majority of men with serologic recurrence after prior local therapy. Further study is needed to determine long-term efficacy of this combination of low dose hormonal therapy.

## DETAIL SUMMARY SHEET

**TITLE:** A Phase II Study to Determine the Effects of Flutamide on Patients with Rising PSAs Who Have Had Radical Prostatectomy, Radiation, or Cryoablation Treatment for Localized Primary Prostate Cancer

**KEYWORDS:** prostate, cancer, flutamide

**PRINCIPAL INVESTIGATOR:** Moul, Judd COL MC

**ASSOCIATES:**

**DEPARTMENT:** Surgery

**STATUS:** O

**SERVICE:** Urology

**INITIAL APPROVAL DATE:** 28 January 1997

### STUDY OBJECTIVE

To determine whether or not the use of low dose flutamide alone in patients with PSA – only recurrent prostate cancer should be advanced to the other studies; mainly a phase III randomized trial. This study is also designed to determine the toxicity of 250 mg flutamide and to determine the likelihood of those patients who were potent upon enrolling into the study to maintain their potency.

### TECHNICAL APPROACH

Patients receive flutamide daily and are followed for two years.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Thirty (30) patients have been enrolled in this study at WRAMC. All adverse events have been reported. A total of seventeen (17) patients have been dropped from the study: seven (7) for diarrhea (an expected side effect), four (4) had progression of the disease and were advanced to full hormonal therapy, one (1) for anxiety, one (1) died, three (3) have moved, and one (1) for other health concerns. All patients have experienced gynecomastia (also an anticipated side effect). The thirteen (13) patients remaining on the study are tolerating the drug and continue to respond. Eight (8) patients have completed the two-year study period and will be followed for survival for five (5) years per protocol. Due to the research drug going generic, the sponsor has closed the study because of lack of funding; subsequently, the principle investigator has closed this protocol to new enrollment.

The number of subjects enrolled to the study since last APR at WRAMC is 1 and the total enrolled to date at WRAMC is 30.

### CONCLUSIONS

None to date.

## DETAIL SUMMARY SHEET

**TITLE:** Retrospective Review of Three-Dimensional (3D) Computerized Tumor Volume Determination in Radical Prostatectomy Specimens From Black and White Patients

**KEYWORDS:** prostate, computerized, tumor volume

**PRINCIPAL INVESTIGATOR:** Moul, Judd COL MC

**ASSOCIATES:** McLeod, David COL MC, Bauer John MAJ MC

**DEPARTMENT:** Surgery

**STATUS:** O

**SERVICE:** Urology

**INITIAL APPROVAL DATE:** 25 November 1997

### STUDY OBJECTIVE

The goal of this study is to compare tumor volume and characteristics of whole-mount radical prostatectomy specimens between black and white prostate cancer patients.

### TECHNICAL APPROACH

This is a retrospective study of the CPDR Prostate Cancer Database examining the tumor volume measurements and tumor locations derived from our whole-mount radical prostatectomies performed by AFIP since April 1993.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are no new literature findings to report, and there have been no amendments or modifications to the research since the last review. There have been no adverse events. No patients have withdrawn from the study.

This study is ongoing. In the last year, we have examined the effect of tumor volume as a prognostic factor for recurrence after radical prostatectomy in black and white patients. Using multivariable analysis tumor volume was examined with other traditional prognostic factors.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 310.

### CONCLUSIONS

Tumor volume is an important prognostic factor for recurrence for black and white men. An additional publication is being prepared to report these new findings.

## DETAIL SUMMARY SHEET

TITLE: Three-Dimensional Ultrasonic Visualization Prostate Cancer

KEYWORDS: ultrasound, 3-D modeling, prostate

PRINCIPAL INVESTIGATOR: Moul, Judd COL MC

ASSOCIATES: McLeod, David COL MC

DEPARTMENT: Surgery

STATUS: C

SERVICE: Urology

INITIAL APPROVAL DATE: 25 November 1997

### STUDY OBJECTIVE

The general objective is to validate current, biopsy-based results indicating that power spectrum analysis of radio-frequency (RF) ultrasonic echo signals from the prostate can distinguish cancerous from non-cancerous prostate tissue in three dimensions (3-D) over the full volume of the prostate. The specific objective is to correlate whole-mount histology obtained from radical prostatectomy specimens with 3-D tissue-typing images derived from RF echo signals obtained immediately prior to prostatectomy.

### TECHNICAL APPROACH

Patients enrolled in this study will already be scheduled for radical prostatectomy. These examinations will use standard TRUS instrumentation and procedures to acquire RF-echo signal data within a week of surgery. RF echo-signal data will be acquired using a currently available B&K Medical systems transrectal prostate scanner. This scanner will be interfaced with a data-acquisition computer using an interface module and digital hardware identical to current units currently utilized in Riverside Research Institutes' (RRI) collaborative study with MSKCC. The examining urologist will acquire RF data from approximately 20, evenly spaced, parallel transverse scan planes for each patient. Sectioning of prostatectomy specimens will be performed by pathologists at AFIP in planes corresponding to the scan planes of the pre-surgical TRUS examination. The pathologist will demonstrate lesion boundaries directly on digital images of each whole-mount section using available image-manipulation software. RRI will process RF data using RRI's current off-line method to generate color-encoded, volume renderings of the prostate. The volume renderings will be compared with whole-mount histology performed on excised glands. Comparisons will be made between computer-generated depictions of lesions and lesion properties determined from histology. This comparison will be based on tumor borders demarcated by the pathologist on images of each section and will assess tumor shape, volume, number of foci, etc. In addition, staging based on lesion features depicted by the 3-D images will be compared to clinical and pathological staging; relative performance will be expressed as ROC curves.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The study was unable to be completed due to technical difficulties with the equipment from the collaborators from MSKCC. Therefore, the protocol was terminated.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is N/A, if multi-site study.

### CONCLUSIONS

There were no conclusions.

## DETAIL SUMMARY SHEET

TITLE: NPCP 2200 - A Comparison of Leuprolide with Leuprolide and Flutamide in Previously Untreated Patients with Clinical Stage D2 Cancer of the Prostate

KEYWORDS: leuprolide, flutamide, prostate cancer

PRINCIPAL INVESTIGATOR: McLeod, David COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: O  
INITIAL APPROVAL DATE: 26 February 1985

### STUDY OBJECTIVE

To try to determine if the antiandrogen flutamide will increase the efficacy of leuprolide.

### TECHNICAL APPROACH

Patients are randomized to receive leuprolide and flutamide or leuprolide and placebo. At the time of progression, the blind is broken, and patients not receiving flutamide will be given drug.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 24. The total number enrolled study-wide is 600, if multi-site study. We are currently following two patients for survival, both of whom are still living.

### CONCLUSIONS:

It was concluded that in patients with advanced prostate cancer, treatment with leuprolide and flutamide is superior to treatment with leuprolide alone.

## DETAIL SUMMARY SHEET

TITLE: NPCP 2200 - A Comparison of Leuprolide with Leuprolide and Flutamide in Previously Untreated Patients with Clinical Stage D2 Cancer of the Prostate

KEYWORDS: leuprolide, flutamide, prostate cancer

PRINCIPAL INVESTIGATOR: McLeod, David COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: C  
INITIAL APPROVAL DATE: 26 February 1985

### STUDY OBJECTIVE

To try to determine if the antiandrogen flutamide will increase the efficacy of leuprolide.

### TECHNICAL APPROACH

Patients are randomized to receive leuprolide and flutamide or leuprolide and placebo. At the time of progression, the blind is broken, and patients not receiving flutamide will be given drug.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 24. The total number enrolled study-wide is 600, if multi-site study. We were following two patients for survival, both of whom are deceased.

### CONCLUSIONS:

It was concluded that in patients with advanced prostate cancer, treatment with leuprolide and flutamide is superior to treatment with leuprolide alone.

## DETAIL SUMMARY SHEET

TITLE: Agent Orange Exposure in Vietnam Veterans and the Risks of Prostate Cancer

KEYWORDS: Agent Orange, prostate, cancer, Vietnam

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: C

SERVICE: Urology

INITIAL APPROVAL DATE: 10 February 1998

### STUDY OBJECTIVE

Using a case control design, this study will evaluate the relationship between exposure to Agent Orange and other herbicides and the risk of prostate cancer among the Vietnam veterans who served in the Army. This study also will be able to determine risk based on the level of exposure to Agent Orange.

### TECHNICAL APPROACH

This is a case controlled study – Subjects will be identified through the CPDR multi-center database (those patients with prostate cancer) and a registry of Vietnam vets maintained at the DVA (controls). Once the study population is identified, a computer assisted telephone survey (CATI) will be conducted. A dietary questionnaire will be mailed to those individuals who complete the telephone survey.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Interviews began in August 1999. 962 interviews have been completed, 214 cases and 748 controls. 800 dietary questionnaires have been mailed to study participants, with 500 of the questionnaires completed and returned by the study participants.

Due to logistical problems with the questionnaires and monetary issues, it was decided to close this protocol even though the data has not been analyzed.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 962. The total number enrolled study-wide is N/A, if multi-site study.

### CONCLUSIONS

None.

## DETAIL SUMMARY SHEET

TITLE: ECOG EST 3886 - Randomized Phase III Evaluation of Hormonal Therapy vs. Observation in Patients with Stage D1 Adenocarcinoma of the Prostate Following Pelvic Lymphadenectomy and Radical Prostatectomy

KEYWORDS: Zoladex, orchietectomy, adenocarcinoma/prostate

PRINCIPAL INVESTIGATOR: McLeod, David COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: O  
INITIAL APPROVAL DATE: 05 February 1998

### STUDY OBJECTIVE

To determine the time to progression and survival in patients with histologically confirmed Stage D1 prostate cancer following radical prostatectomy and pelvic lymphadenectomy treated with no immediate hormonal therapy compared to those treated immediately with hormonal therapy.

### TECHNICAL APPROACH

This is a multicenter randomized Phase III trial. Patients can be randomized to hormonal therapy or observation. Those patients randomized to observation may be registered to receive hormonal therapy if their disease progresses. All patients that progress on hormonal therapy will be followed off study drug. This study was closed to enrollment in 1993.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 87, if multi-site study. One patient is followed for survival data. He receives his care at Walter Reed and continues to receive Zoladex off protocol.

### CONCLUSIONS

None at this time.



## DETAIL SUMMARY SHEET

TITLE: Multicenter Prostate Cancer Database for the Center for Prostate Disease Research (CPDR) with Patterns of Care, Outcome and Prognostic Analysis

KEYWORDS: CPDR, prostate, cancer

PRINCIPAL INVESTIGATOR: Moul, Judd COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: O  
INITIAL APPROVAL DATE: 26 May 1998  
MASTER PROTOCOL

### STUDY OBJECTIVE

To maintain an accurate, reliable, secure relational database so as to demonstrate and coordinate longitudinal prostate cancer data collection as part of a multi-center DOD prostate cancer repository at USUHS. To use the database to analyze patterns of care, prognostic factors and intermediate and long-term outcomes for prostate cancer. The CPDR database is suitable for analyzing epidemiological features of prostate cancer and treatment efficacy, and monitoring the quality of life of our patients. Our long-term goal is to have 20,000 patients followed for twenty years.

### TECHNICAL APPROACH

Our goals and objectives will be achieved by: Retrospectively collecting standardized data on all prostate cancer patients treated at specified military medical centers during the period 1960-1997 (under WU#2898). Prospectively by collecting standardized data on all prostate cancer patients treated at specified military centers beginning in 1998. Prospective data collection will be with consent.

On 15 July 2002 exception to policy was approved to increase enrollment for the protocol from 5,000 patients to 8,000 patients. On 10 January 2003 addendum 27 was approved. This allows the entering of the date of death for those in the database that gave verbal consent under the original database protocol and never signed a consent form. Under this protocol we are allowed to keep those patients but cannot enter any data from after 1998.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Main protocol: The database has archived 445,740 clinical records on 17,817 men. The number of TRUS, biopsy, medical history, primary staging, radical prostatectomy, and necropsy records were 21698, 20692, 15195, 13469, 6205, 3453, respectively.

The number of subjects enrolled to the study since last APR at WRAMC is 412 and the total enrolled to date at WRAMC is 5413. The total number enrolled study-wide is 17,817, if multi-site study.

Conclusions: Radical prostatectomy is currently the most common treatment modality for military men with prostate cancer. More than two-thirds of patient mortality is due to non-prostate causes. Disease free survival in patients who underwent radical prostatectomy is improved.

WU# 2857-98 (01, 21, 24)

STATUS: O

TITLE: Retrospective Review of the Changing Face of Prostate Cancer in the 1990s.

### STUDY OBJECTIVE

To explore trends in the military health-care experience with prostate cancer in the 1990s.

#### TECHNICAL APPROACH

(01) Our objectives will be achieved by collecting the following data for the calendar years 1990 thru 1997:

The number of patients diagnosed with prostate cancer between.

Taking the number of new stage D patients (D1 and D2) diagnosed and dividing that number by total number of cases to provide a percentage of stage D per year.

The percentage of cases stratified by Gleason score (Sum): 2-4, 5-6, 7, and 8-10.

The percentage of patients who were diagnosed with clinical T1c disease.

The number of patients with: Clinical stage a + B (T1 and T2), Clinical stage C (T3), Clinical stage D (Tang N + and/or M +).

The median age at diagnosis of the patients diagnosed.

The percentage of patients having primary treatment: radical prostatectomy alone; radiation therapy (external and brachytherapy) alone; primary hormonal therapy alone; watchful waiting (no treatment); combination treatment (i.e. NHT + RP and NHT + XRT).

The mean, median, and range of PSA values at the time of diagnosis for patients diagnosed.

The racial composition of patients.

(21) The following additions were made with this amendment:

Include data from 1988-1998.

Patients' most recent follow-up date.

Patients' date of consent.

If patient died, date of death and cause of death.

Pathologic stage of patients undergoing radical prostatectomy: a) seminal vesicle status b) margin status c) capsule status d) Gleason sum in radical prostatectomy specimen e) tumor grade in radical prostatectomy specimen f) volume of tumor in radical prostatectomy specimen g) number of tumors in radical prostatectomy specimen.

Date of recurrence of prostate cancer after primary treatment.

Tumor grade, on biopsy, or all patients diagnosed between 1988 and 1998.

(22) The following additions were made with this amendment:

To broaden the epidemiological data from the PSA era, which started in 1988, data from 1988 through 2000 will be used.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found.

The most important finding of this study is the significantly increased five-year disease-specific survival, and overall survival, when comparing early, mid, and later PSA era patients. This parallels the work of Gilliland et al. who showed improved survival during a period of PSA screening in New Mexico using the SEER (Surveillance, Epidemiology and End Results Program of the National Cancer Institute) data. The SEER five-year relative cancer survival rates for patients diagnosed in the following year groups: 1974-1976, 1980-1982, and 1989-1995 were 67%, 73%, and 92%; each of these changes were statistically significant ( $p < 0.05$ ). The critics of PSA testing argue that the benefits of screening are merely a result of lead-time bias. However, Etzioni et al. have determined that the improved survival is not due simply to PSA testing, even if one considers a very short lead-time of three years.

Other factors such as increased public awareness and the increased use of hormone therapy in patients with metastatic disease may also be affecting survival and mortality. The percentage of deaths due to prostate cancer has decreased in the more recent year groups. This effect emphasizes the improved survival of patients diagnosed in more recent year groups, and suggests that patients diagnosed in the PSA era are more likely to live longer and die of other causes, rather than dying of prostate cancer. Unfortunately, only after the results of ongoing screening trials become validated, will the survival benefits of PSA testing become truly evident.

We have demonstrated a significant stage migration. Most strikingly, the percentage of patients presenting with metastatic disease decreasing from 14.1% and 19.8% in 1988 and 1989, respectively, to 3.3 % in 1998. Before a survival benefit, a decrease in metastatic disease should be evident; which is clearly being shown on a national level by several studies. These findings are more impressive in light of the fact that no curative treatment exists for patients with metastatic disease. Similarly, there was a statistically significant decrease in the incidence of clinical

T3 and T4 disease. PSA-testing is reclassifying many of these tumors as T1c, which is associated with decreased recurrence rates, and increased disease-specific survival, when compared to other clinical stages.

The percentage of tumors that have a clinical stage of T1a and T1b has decreased. This is most likely a result of medical management of benign prostatic hyperplasia (BPH) and the use of PSA screening. Patients with BPH, and an elevated PSA, will undergo a transrectal ultrasound (TRUS) and biopsy of the prostate, prior to transurethral resection of the prostate (TURP). This often results in the discovery of T1c cancers, and subsequent stage reclassification. A recent comprehensive review of TURP shows that the chance of discovering cancer on TURP is 6%, down from over 20% prior to the PSA era.

### CONCLUSIONS

Data from this study indicates that during the PSA era there has been a statistically significant improvement in survival which is most likely secondary to a clinical stage migration from metastatic disease to disease that is amenable to curative treatment. In addition the chance of a patient dying of prostate cancer had decreased dramatically over the thirteen years of the study (1988-2000). Continued follow-up of these patients is mandatory to further delineate the improvements in patient outcomes that have been achieved during the PSA-era.

Comparing 1988-89, with 1998-99: The percentage of African American (AA) men with extracapsular extension (ECE) decreased from 100%, to 34.8% ( $p=0.007$ ), and for Caucasians from 56.9%, to 43.2% ( $p=.269$ ). The percentage of AA men with positive margins decreased from 100%, to 26.1% ( $p<0.001$ ), and for Caucasians from 41.2%, to 27.0% ( $p=0.021$ ). Mean age at surgery decreased from 66.6 to 59.9 years for AA ( $p<0.001$ ), and from 65.9 to 61.1 years for Caucasians ( $p<0.001$ ). Mean PSA level (1990 to 1999) decreased from 16.5 to 6.5 ng/dl for AA men ( $p<0.001$ ), and from 10.1 to 6.6 ng/dl for Caucasians ( $p<0.001$ ).

We believe that the striking decrease in ECE and positive margins in AA men is due to PSA testing, coupled with improved public awareness, and equal access to care. It appears reasonable to recommend PSA testing in AA men, who have historically experienced poor outcomes from prostate cancer. This amendment has broad objective and the intention is to continue to track changes in trends.

WU# 2857-98 (05)

STATUS: O

TITLE: Erectile Dysfunction in Patients with Prostate Cancer

### STUDY OBJECTIVE

Research on the side effects of prostate cancer treatment has been largely focused upon the absolute number of side effects (incontinence, impotence or bladder neck contracture) of surgery or radiation therapy, but has not evaluated the effectiveness of the treatments rendered. The widespread availability of prostheses, infection therapy and oral medications create new dilemmas in the proper treatment of post-prostate cancer erectile dysfunction. All of these treatments incur additional costs for the care of prostate cancer patients. In most health care reimbursement systems, these costs are not covered by the health care plans. Collection data on the pre- and post-treatment rates of erectile dysfunction and comparing the effectiveness of various treatments may give clinicians valuable insight into the most effective treatment options. This information will assist clinicians and patients in making these very important decisions, and the cost-effectiveness created by avoiding treatments with low likelihood of success will provide increased resources throughout the health care system.

### TECHNICAL APPROACH

The following data points will be collected and analyzed: Unique patient identifier, age, date of birth, diagnosis date, pathology, primary treatment, pre-treatment potency, follow-up dates, follow-up potency. Erectile Dysfunction (ED) treatment used, Effectiveness of the ED treatment.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found. Current progress: no significant difference was noted in the post treatment erectile function between patients treated with radical prostatectomy of external beam radiation (10% vs. 15%). Patients selecting watchful waiting heavy the lowest risk of erectile

dysfunction. Clinical stage and race were significant predictors of the development of erectile dysfunction in the watchful waiting and external beam radiation treatment groups

### CONCLUSIONS

Erectile dysfunction develops in greater than 80% of patients treated for prostate cancer. External beam radiation has the same risk for erectile dysfunction as radical prostatectomy. We want to assess Viagra and other treatments for impotence outcomes next

WU# 2857-98 (07)

STATUS: C

TITLE: The Utility of Computed Tomography and Bone Scan to Identify Residual Disease in Patients with an Elevated Serum Prostate Antigen After Radical Prostatectomy

### STUDY OBJECTIVE

Radical prostatectomy is a common treatment for localized prostate cancer. Approximately 15% of patients with pathologically localized prostate cancer and 50% of patients with locally extensive disease will have a rising prostate specific antigen (PSA) within ten years. A bone scan and abdominopelvic CT are commonly performed to attempt to classify patients as locally recurrent disease vs. metastatic disease. This study will attempt to define the usefulness of these radiographic studies in this clinical situation. It is suspected that the studies are of low utility, and many patients may be spared the cost and inconvenience of having them performed.

### TECHNICAL APPROACH

A retrospective analysis of the CPDR database will be performed identifying all patients who underwent RP between 1988 and 1998 who have suffered a PSA recurrence. The patients will be entered into a database and CHCS will be queried to determine if they underwent a bone scan and/or a CT. The results of those studies will be obtained and entered into a database. The likelihood of the radiographic studies being positive and the nature of the abnormality will be analyzed. The following data will be collected: 1) Name, Initials or SSN; 2) Ethnicity; 3) Age at diagnosis; 4) PSA at diagnosis; 5) Grade at diagnosis; 6) Clinical stage; 7) Date of surgery; 8) Pathologic stage; 9) Pathologic Grade; 10) Date of PSA recurrence; 11) PSA values and dates – most recent three prior to hormonal therapy; 12) Clinical recurrence; 13) Bone scan results: Positive, negative, equivocal – if positive site of abnormality; 14) CT scan results: Positive, negative, equivocal for local or distant Cap recurrence – if positive site of recurrence 15) Type of adjuvant therapy: XRT, HT, observation, other.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found.

To define the utility of bone scan and computed tomography (CT) in the evaluation of patients with biochemical recurrence after radical prostatectomy. A retrospective analysis of the Center for Prostate Disease Research database was undertaken to identify patients who underwent radical prostatectomy between 1989 and 1998. Patients who developed biochemical recurrence (two prostate-specific antigen [PSA] levels greater than 0.2 ng/mL) and underwent either bone scan or CT within three years of this recurrence were selected for analysis. The preoperative clinical parameters, pathologic findings, serum PSA levels, follow-up data, and radiographic results were reviewed. One hundred thirty-two patients with biochemical recurrence and a bone scan or CT scan were identified. Of the 127 bone scans, 12 (9.4%) were positive. The patients with true-positive bone scans had an average PSA at the time of the bone scan of 61.3 +/- 71.2 ng/mL (range 1.3 to 123). Their PSA velocities, calculated from the PSA levels determined immediately before the radiographic studies, averaged 22.1 +/- 24.7 ng/mL/mo (range 0.14 to 60.0). Only two patients with a positive bone scan had a PSA velocity of less than 0.5 ng/mL/mo. Of the 86 CT scans, 12 (14.0%) were positive. On logistic regression analysis, PSA and PSA velocity predicted the bone scan result ( $P < 0.001$  each) and PSA velocity predicted the CT scan result ( $P = 0.047$ ). Patients with biochemical recurrence after radical prostatectomy have a low probability of a positive bone scan (9.4%) or a positive CT scan (14.0%) within three years of biochemical recurrence. Most patients with a positive bone scan have a high PSA level and a high PSA velocity (greater than 0.5 ng/mL/mo).

### CONCLUSIONS

Patients with biochemical recurrence after radical prostatectomy have a low probability of a positive bone scan (9.4%) or a positive CT scan (14.0%) within three years of biochemical recurrence. Most patients with a positive bone scan have a high PSA level and a high PSA velocity (greater than 0.5 ng/mL/mo).

WU# 2857-98 (08)

STATUS: O

TITLE: Review of the Prostatic Intraepithelial Neoplasia (PIN) in Prostatectomy Specimens Pre-Treated with Neoadjuvant Hormonal Therapy (NHT)

### STUDY OBJECTIVE

The goal of this study is to:

a) Determine how often PIN is present and how extensive it is in patients treated with hormonal therapy prior to surgery versus those treated with surgery alone; b) Compare the histologic features of the PIN to that of the coexisting invasive carcinoma, particularly with respect to the extent of treatment effect; c) Determine, by immunohistochemistry, if PIN is still capable of progression utilizing the standard monoclonal antibody MIB-1 which is a routine marker of used proliferative activity d) Evaluate the presence of neuroendocrine cells in the detectable carcinomas and PIN by immunohistochemistry (chromogranin, a standard routine non-investigational stain).

### TECHNICAL APPROACH

Retrospective data on all AFIP-referred RP patients who were treated at WRAMC and NMCS D between 1993 and 1998 will be studied. The following information will be gathered: 1) AFIP Accession Number; 2) Race; 3) Age at diagnosis; 4) Start and stop date for hormonal therapy (LHRH start and stop dates, Antiandrogen start and stop dates, Orchiectomy date); 5) Surgery date; 6) Clinical Stage and TNM clinical stage: A, B, C; T1, T2, T3; 7) Total number of tumors in radical prostatectomy specimen; 8) Total tumor volume in radical prostatectomy specimen (as performed in WU#2834); 9) Pre-treatment PSA value (ng/ml); 10) Surgical Margin status: Positive, Negative; 11) Benign Glands in Margin: Yes, No; 12) Path Gleason Score: 2-10 (worst Gleason sum in radical prostatectomy); 13) WHO differentiation: Well, Moderate, Poor; 14) Nuclear Grade: I, I-II, II-III, III; 15) PSA Recurrence: Yes, No; 16) Date PSA Recurrence; 17) Clinical Recurrence: Yes, No; 18) Date Clinical Recurrence; 19) Last Follow-up Date; 20) Last PSA Value and Date.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

In 9 of 26 prostatectomy specimens, PIN was detectable. In two patients, both PIN and tumor exhibited no appreciable proliferative activity, in three both tumor and PIN had a high proliferation rate. In three patients the tumor had a higher proliferation index than the PIN.

Of the nine prostate specimens with PIN, only one retained high proliferative activity of the PIN following treatment. In six of the nine patients, tumor and PIN showed the same proliferation rate following androgen ablation. PIN was recognizable in three of the four patients with high proliferative activity in the tumors. But in two of these, the proliferative activity was low or minimal in the PIN. These findings may indicate a greater sensitivity of PIN to androgen blockade.

### CONCLUSIONS

None at this time.

WU# 2857-98 (13)

STATUS: O

TITLE: Can Seminal Vesicle Invasion of CaP Predict Disease Progression

### STUDY OBJECTIVE

It has been observed that patients who have Seminal Vesicle (SV) invasion have a worse prognosis. This study will look at the extent of SV invasion within the CPDR database to see if the magnitude has any bearing on recurrence of disease within the patient population.

#### TECHNICAL APPROACH

The surgical pathology reports and PSA post radical prostatectomy data will be reviewed to determine how many people have SV invasion. After defining who has SV invasion, the data will be analyzed to determine if prostate cancer disease progression can be predicted according to the amount of SV invasion that is present.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found.

505 prostatectomies obtained from 1993-1999 sectioned at 2.2mm intervals were processed as whole-mounts. All tumors with pathologic stage 3b and four were reviewed for the pattern of SVI as reported by Ohori et al. The pattern and extent of SVI were correlated with tumor grade, surgical margin status, vascular invasion and post-operative biochemical progression.

Three of 53 patients showed SVI along the ejaculatory ducts (type I). In 34 cases SVI occurred through the capsule with or without ejaculatory duct involvement (type II or type I and type II). In 16 cases, SVI occurred with our direct connections to the main tumor (type III). Vascular invasion was observed in 22 patients. Surgical margins were positive in 35 patients. In 41 patients, extraprostatic extension was present in other sites that SVI. All but four patients had poorly differentiated elements that exceeded 25% of the tumor in 21 patients. In 12 patients, SVI did reach the attachment site. None of the patients with type I SVI recurred. Seventeen of 34 patients with type II or I and II, SVI recurred. Six of these showed vascular invasion. Of the 16 patients with type III SVI, six recurred. 33% of patients with SVI up to the attachment site recurred vs. 46.3% extending into the free part of the SV. We found no difference with respect to progression considering the presence of vascular invasion.

#### CONCLUSIONS

When SV is invaded from the prostate, progression appears to be lower than when it is due to capsular penetration of "metastatic" spread. We did not observe any difference in progression rate when comparing type II or I and III to type III invasion.

WU# 2857-98 (14)

STATUS: O

TITLE: Time to NADIR of Serum Prostate Specific Antigen (PSA) for Patients with Prostate Cancer Treated with Radiotherapy

#### STUDY OBJECTIVE

Several surrogate endpoints have been proposed for patients with CaP after definitive therapy because of the long natural history of the disease in most cases. PSA nadir values have received most attention, but no time to nadir has been proposed as a surrogate that better incorporates kinetics of PSA half-life. Some studies have reported that patients who ultimately fail therapy reach higher nadir values earlier than patients who remain without evidence of disease (NED); other reports state that time to nadir is not related to outcome.

#### TECHNICAL APPROACH

The following data from all curative radiotherapy patients (excluding: post prostatectomy; if hormonal therapy was provided before radiation therapy) between 1 January 1992 and 31 December 1994 will be analyzed: age; stage; grade; PSA date and value closest to XRT therapy start date, all PSA values and date post-XRT; XRT treatment date (dose, # fractions, # days, technique, date therapy was completed); date of last follow-up; date of hormonal treatment; date of death.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found.

The multicenter data query is pending while the data holes are identified and filled.

#### CONCLUSIONS

None at this time.

WU# 2857-98 (15)

STATUS: O

TITLE: Prostate Specific Antigen (PSA) Response After Combined Temporary Androgen Suppression and External Beam Radiotherapy

#### STUDY OBJECTIVE

The American Society for Therapeutic Radiology and Oncology (ASTRO) Consensus Panel definition for biochemical failure following external beam radiation therapy for prostate cancer is three consecutive increases in PSA. In recent years, temporary androgen suppression has been combined with external beam radiotherapy as curative therapy for localized prostate cancer. There is almost always an excellent PSA response with this combination, but it is not uncommon for the PSA to rise to some degree once androgen suppression has been stopped. The purpose of this study is to test the validity of the ASTRO definition of biochemical failure in patients treated with combined androgen suppression and radiotherapy.

#### TECHNICAL APPROACH

The following data from all patients treated with curative intent for prostate cancer with temporary androgen suppression and external beam therapy (excluding: post prostatectomy; if the androgen suppression therapy was > 12 months which does not exclude patients who subsequently fail and were then placed on long term hormonal therapy) between 1 January 1986 and 31 December 1996 will be analyzed: Age at Diagnosis; Clinical stage (AJCC); Tumor grade (Gleason score); PSA date and value prior to any therapy (pretreatment PSA), All PSA dates values after radiotherapy; Radiation therapy treatment (Total dose, Technique, # fractions and # of days, date therapy was started and completed); Dates and type of hormonal therapy(dates and dose, 1 or 3 months, of LHRH agonist injections; start and end dates of antiandrogen (flutamide, Casodex)); Date and site of clinical failure (i.e. bone scan, re-biopsy, etc.); date and type of subsequent therapy; Date of last follow-up; Date of death.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found.

The multicenter data query is pending while the data holes are identified and filled.

#### CONCLUSIONS

None at this time.

WU# 2857-98 (20)

STATUS: O

TITLE: Comparison of Disease Free Survival and Overall Survival of Patients with Carcinoma of the Prostate Treated with Radical Prostatectomy of Radiation Therapy in the PSA Era

#### STUDY OBJECTIVE

The CPDR database is unique, in that it contains longitudinal data on patients treated for CaP from 1988-1999 in the military health care system at 10 different medical facilities. The goal of this protocol is to retrospectively examine patients that were primarily and solely treated with RP or XRT between 1988-1994. The subjects will be stratified for tumor grade, Gleason sum, clinical stage, ethnicity, age, pre-biopsy and/or pre-treatment PSA to determine if there is a statistically significant difference in DFS, development of distant metastasis, and/or death from CaP between these two groups (XRT and RP) with a minimum of a five year follow-up (1995-1999). The study will also determine if margin status, in those patients that underwent RP, is an independent predictor for PSA recurrence, DFS, distant metastasis, and mortality. The study will examine the dose of radiation given to see if that is an independent predictor of DFS, distant metastasis or mortality. The results of this study will help inform clinicians on how to counsel patients, with various pre-treatment criteria, on which from of treatment, XRT or RP, may be best suited to them.

#### TECHNICAL APPROACH

This study will use multivariate Cox regression analysis to determine significant pre-treatment variables for both XRT and RP for DFS, development of distant metastasis, and death from CAP. Also, regression analysis will be used to determine if age, medical history, margin status, pathologic stage, and particularly primary treatment (XRT or RP) are an independent predictor of DFS, development of distant metastasis, and death.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found.

Between 1988 and 1994, 969 patients were treated with either radical prostatectomy or conventional dose external beam radiation at WRAMC. 915 (94.4%) of these patients had adequate information available for analysis. Retrospective review of follow-up data from patient charts, the hospital clinical computer system, and the CPDR database was performed. After treatment was administered, follow-up occurred at a frequency determined by the patient's individual physician. PSA recurrence was defined by the ASTRO criteria for RT patients and as a PSA  $\geq$  0.4 for the RP patients. Hormone therapy for clinical or biochemical progression was instituted at physicians' discretion and bone scans were obtained when directed by the physician. Average length of follow-up in this study was 113 months in the RT group and 114 months in the RP group.

CONCLUSIONS – Preliminary:

**RESULTS:** Four hundred eighty (52.3%) patients received RT while 435 (47.7%) underwent RP. Two hundred thirty-five (49%) of the RT patients and 176 (40.5%) of the RP patients experienced biochemical recurrence with an average time to recurrence of 28.8 months (range 1.3-98.1) and 38.3 months (range 0.7-152.0), respectively. Thirty-five (29.4%) low-risk RT patients and 35 (20.3%) low-risk RP patients had biochemical recurrence with an average time to recurrence of 34.8 months (range 5.0-68.5) and 40.7 months (range 1.8-94.9), respectively. Two hundred (55.4%) high-risk RT patients and 141 (53.6%) high-risk RP patients recurred at an average of 27.7 months (range 1.3-98.1). Our data suggest that RP is a better treatment option than conventional dose RT for patients whether they are low or high-risk. We use a mature database depicting patients undergoing similar treatment at a single institution with similar follow-up in the PSA era with long follow-up times. This study serves as a valid basis for RT protocols employing dose escalation even for low risk patients and consideration of neoadjuvant or adjuvant hormonal therapy approaches. To determine whether these approaches will result in outcome equivalence to RP will require further study.

WU# 2857-98 (23)

STATUS: O

TITLE: Retrospective Review of Prostate Needle Biopsy Site to Predict Radical Prostatectomy Margin Status

STUDY OBJECTIVE

Surgery is often preferred therapy for young patients with early stage prostate cancer (CaP) because of relatively higher rate of biochemical disease-free survival than after radiotherapy. Unfortunately, the effect of young age on outcome after therapy for CaP has been infrequently reported on the surgical literature and even less frequently reported in the radiotherapy literature. This protocol will document outcomes after radiotherapy in young men; specifically defined as  $\leq$  59 years old at diagnosis. Subset analysis will be reported for men  $\leq$  55 years, and if sufficient data exists,  $\leq$  50 years. These will be compared with surgical outcomes once patients are matched by pretreatment Gleason score, pretreatment clinical stage, and pretreatment PSA.

TECHNICAL APPROACH

Data will be analyzed for relationships between location of positive biopsy and location of positive margin on RP specimens, impact of nerve sparing and its relationship to positive biopsy location, margin status and number of biopsies, margin status and size of prostate gland, margin status and Gleason score and margin status and pre-tx PSA. Data will then be analyzed by a statistician using a univariate and multivariate regression analysis.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found.

The multicenter data query is pending while the data holes are identified and filled.

CONCLUSIONS

The study is ongoing and there are no conclusions at this time.



## DETAIL SUMMARY SHEET

TITLE: SWOG 8894 - A Comparison of Bilateral Orchiectomy With or Without Flutamide for the Treatment of Patients with Histologically Confirmed Stage D2 Prostate Cancer

KEYWORDS: cancer, prostate, orchiectomy

PRINCIPAL INVESTIGATOR: McLeod, David COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: O  
INITIAL APPROVAL DATE: 05 February 1998

### STUDY OBJECTIVE

To test the hypothesis that total androgen blockade (orchiectomy plus flutamide) may be better than orchiectomy alone.

TECHNICAL APPROACH (Describe the methodology and note any modifications.)  
This is a prospective, randomized, double blind, placebo controlled study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 35. The total number enrolled study-wide is 1387, if multi-site study. Two patients are being followed for survival data. One patient is receives his care at WRAMC and is living with metastatic prostate cancer, the other patient receives his care at a civilian clinic and is disease-free at this time.

### CONCLUSIONS

The combined androgen blockage (CAB) benefit is clinically negligible.

## DETAIL SUMMARY SHEET

TITLE: ECOG P-Z887 - A Phase I Study of Intravesical Tumor Necrosis Factor in the Treatment of Superficial Bladder Cancer

KEYWORDS: intravesical, tumor necrosis factor (TNF), bladder cancer

PRINCIPAL INVESTIGATOR: McLeod, David COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: C  
INITIAL APPROVAL DATE: 05 February 1998

### STUDY OBJECTIVE

To determine: 1) safety of TNF instilled into the bladder as an intravesical form of therapy for superficial bladder cancer; 2) the scope and severity of toxicity of the TNF in patients with bladder cancer; 3) the dose limiting toxicities and maximum tolerated dose of TNF; 4) any systematic effects of the TNF on other organ systems and to determine systemic pharmacokinetics.

### TECHNICAL APPROACH

Three patients will be treated at each dose level (200-250 mcg.) Each patient will receive all treatments of TNF in a single dose level. If DLT is seen in more than one patient, an additional three patients will be entered at this dose level. If a total of three of these six patients exhibit a DLT, then dose escalation will end and all subsequent patients will be entered at this dose level.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 3. The total number enrolled study-wide is unavailable, if multi-site study. Per ECOG correspondence dated 06 Jun 02, patients will no longer be followed for survival data. The study was closed by ECOG in 1991 due to poor accrual. We are following two patients for survival, both of whom are currently living. The third patient died.

### CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: ECOG EST 9887 - A Phase III Trial of Treatment of Pathologic Stage C Carcinoma of the Prostate with Adjuvant Radiotherapy

KEYWORDS: prostate, cancer, adjuvant radiotherapy

PRINCIPAL INVESTIGATOR: Moul, Judd COL MC

ASSOCIATES: McLeod, David COL MC

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: O

INITIAL APPROVAL DATE: 05 February 1998

### STUDY OBJECTIVE

To compare in a randomized study, the disease-free survival rates in completely resected patients with pathologic Stage C (T3Noh10) carcinoma of the prostate assigned to be treated with adjuvant external beam radiotherapy to that in patients assigned to receive no adjuvant therapy. To assess the qualitative and quantitative toxicities of patients with pathologic Stage C carcinoma of the prostate when treated with external beam radiotherapy.

### TECHNICAL APPROACH

After prostatectomy with pelvic lymphadenectomy and no evidence of regional lymph node or metastatic disease, the patient is randomized to receive adjuvant radiation therapy or no adjuvant therapy. All patients are off treatment 1 year after randomized or at disease progression.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 4. The total number enrolled study-wide is unavailable, if multi-site study. This ECOG protocol has been closed to enrollment since 1996 due to poor accrual nationwide. We are currently following 2 patients for survival status. Two patients live outside of the Walter Reed health care system and receive their care elsewhere. They are contacted yearly for survival information and are both in excellent health at this time. The remaining two patients have died.

### CONCLUSIONS

None available at this time.

## DETAIL SUMMARY SHEET

TITLE: Creation of a Tissue Library for the Molecular Biologic Study of Patients with Prostate Cancer

KEYWORDS: prostate, cancer, tissue

PRINCIPAL INVESTIGATOR: Moul, Judd COL MC

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: O

INITIAL APPROVAL DATE: 21 July 1998

MASTER PROTOCOL:

### STUDY OBJECTIVE

To create a tissue library for the molecular biologic study of prostate cancer.

Develop a primary and immortalized cell cultures from prostate cancer specimens.

Define the role that oncogenes and tumor suppressor genes play in the progression of prostate cancer.

Analyze genetic susceptibility factors for prostate cancer such as androgen receptor CAG repeats and HPCI mutations.

Correlate RNA and DNA molecular biology assays to the ongoing clinical database (WU # 2898). Create a 3-dimensional reconstruction of the prostate gland to assess the volume of all individual tumors, their locations within the prostate gland, their molecular pedigree and any extracapsular extension of the neoplasm.

### TECHNICAL APPROACH

Samples will be obtained from TURP and radical prostatectomy specimens that will include cancerous and normal tissue. Informed consent will allow interoperative collection of blood, bone marrow, and tissue biopsies of the excised organ. It will allow the use of these specimens as well as the retrieval and use of their original archival biopsy tissue. Blood samples will be used to measure specific molecular markers and will be compared to clinical features. All samples will be processed by AFIP using SOP, and sent to the CPDR lab as required.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and there is nothing new to report. There are no AEs to report. The updated consent form was approved by the HUC 2/25/03 to include language requested by DCI.

The number of subjects enrolled to the study since last APR at WRAMC is 94 and the total enrolled to date at WRAMC is 651.

### CONCLUSIONS

WU# 2871-98 (01)

STATUS: O

TITLE: Involves Spectral Karyotyping and collaboration with Dr. Kenneth Carter - no subtitle given for this amendment

### STUDY OBJECTIVE

Perform Spectral Karyotyping (SKY) analysis and identification of genetic alterations in prostate samples.

### TECHNICAL APPROACH

Cultured cells will be harvested and fixed on glass slides using standard techniques for chromosome preparation. The prepared slides will be transferred to the International Genetics Associates (IGA), Inc. for SKY analysis.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Carcinoma of the prostate (CaP) is the second most important cause of cancer mortality among males, yet our understanding of the biology of CaP progression and its molecular correlates is limited. An understanding of genetic changes in prostate cancer would have obvious clinical value, as well as pointing to candidate targets for the

development of new therapeutics. Although gene alterations characteristic of CaP, including up-regulation of oncogenes and mutations in tumor suppressor genes, have been described (reviewed in Karan, '02), it is not known which of these alterations play critical roles in determining clinical outcomes, nor how these mutations correlate with tumor progression. While several metastatic cell lines have been used extensively in CaP research, the availability of primary CaP model systems that reflect the genetic and phenotypic heterogeneity of clinical prostate cancer has been limited. We report here the characterization of ten primary prostate cancer cell lines (CPDR1 through CPDR 10) derived from sporadic CaP by immortalization with the human papilloma virus (HPV) E6 and E7 genes. Some of the genetic alterations characteristic of these ten cell lines were present not only in the source lesion but also in a multi tumor tissue microarray constructed from the whole prostate from which they were originally derived. This level of genetic similarity suggests the relative stability of the changes detected, and the potential relevance of the cell lines for use in drug discovery for CaP. Comparison of the genetic signatures of these primary CaP cell lines with clinical prostate cancers not only validates the utility of the lines but could also contribute to the identification of prostate-specific gene targets and the development of novel anti-cancer therapies.

#### CONCLUSIONS

None at the time of this APR.

WU# 2871-98 (03)

STATUS: O

TITLE: Genetic Susceptibility to Prostate Cancer

#### STUDY OBJECTIVE

To test the hypothesis that genes which regulate the levels of circulating testosterone and the bioactivation of heterocyclic amines predispose individuals to the development of prostate cancer.

#### TECHNICAL APPROACH

Dr. Reynolds at the Center will test samples for Disease Control - National Institute of Occupational safety and Health. 200 prostate cancer patients and 200 age-matched controls will be evaluated for CYP17 and NAT2 genotypes by combination of PCR gene amplification (normal/3' mismatch) and restriction enzyme digestion. Individual genotypes (CYP17 or NAT2) and combination genotypes (CYP17 and NAT2) will be analyzed for association with susceptibility or resistance to prostate cancer.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

162 prostate cancer (PC) samples, 164 benign prostatic hyperplasia (BPH) samples and 73 age-matched random control samples have been analyzed for both NAT2 and CYP17 genotype. All 399 samples have been identified by race (Caucasian or African-American). No significant difference in distribution of polymorphisms in the NAT2 gene was found between the Caucasian and African-American populations. The incidence of the A1/A1 allele of CYP17 was higher in the control group (45%) than in the PC (38%) and BPH (41%) groups. However, the difference was not statistically significant. The distribution of the A1/A1 allele was significantly higher in the Caucasian group (44.1%) than in the African-American group (31.4%). These results indicate that polymorphisms in the NAT2 and CYP17 genes may not convey susceptibility to the development of prostate cancer.

#### CONCLUSIONS

None at the time of the APR.

WU# 2871-98 (04)

STATUS: O

TITLE: The Polygenic Model of Prostate Cancer Risk Focusing on Polymorphisms in Multiple Genes Involved in Androgen Signaling

#### STUDY OBJECTIVE

To validate the hypothesis that polymorphisms in multiple genes confers higher risk for prostate cancer than does polymorphism in one gene alone.

#### TECHNICAL APPROACH

We have proposed to study the polygenic model of prostate cancer risk focusing on polymorphisms in multiple genes involved in the androgen signaling. Known polymorphisms in four genes involved in the androgen metabolism/signaling pathways were proposed for analysis including 1) CYP3A4, involved in the deactivation of testosterone; 2) SRD5a2, involved in the conversion of testosterone to dihydrotestosterone; 3) androgen receptor (AR), involved in the regulation of growth of the prostate; and 4) prostate specific antigen (PSA), a prostate specific gene. We will isolate genomic DNA from peripheral blood lymphocytes of normal and prostate cancer subjects using Qiagen tip 100 using manufacturer's protocol (Qiagen Inc. Valencia, CA). We will use this DNA in PCR reactions for genotyping CYP3A4, SRD5A2, PSA and AR using published procedures.

CYP3A4: variant detection (AA, AG and GG variants) will be performed by the TaqMan assay, originally described by Paris PL et al (Cancer Epidemiology Biomarkers & Prevention 8, 901-905, 1999). Specific primers used for amplification of this gene are 5'-ATCTGTAGGTGTGGCTTGTGG-3' (forward primer) and 5'-TATCAGAAACTCAAGTGGAGGCAT-3' (reverse primer). Labeled primers for detecting the polymorphisms in this gene will be 5'-TTAAATCGCCTCTCTCTTGTCTCTAT-3' (FAM-labeled) and 5'-AATCGCCTCTCTCTGCCCTTGTCTCTAT-3' (TET-labeled).

SRD5A2: A49T and V89L variants will be detected following the protocol by Jaffe JM et al (Cancer Research 60, 1626-1630, 2000). The primers used for amplification of this gene are 5'-GCAGCGGCCACCGGCGAGG-3' (forward primer) and 5'-AGCAGGGCAGTGCCTGCACT-3' (reverse primer). Upon completion of thermocycling, the PCR product will be subjected to restriction enzyme fragment analysis. The V89L variant will be identified with RsaI and the A49T variant will be identified with MwoI.

PSA: gene variants (AA, AG, GG genotypes) will be identified as described by Xue et al (Cancer Research 60, 839-841, 2000). The polymorphic site in the prostate specific antigen will be amplified with forward primer (5'-TTGTATGAAGAATCGGGGATCGT-3') and reverse primer (5'-TCCCCAGGAGCCCTAAATAAAA-3'). The PCR product will be digested with NheI restriction enzyme for identifying the three genotypes.

The CAG repeat length of the AR gene will be estimated by Giovannucci E et al (Proc. Natl. Acad. Sci. USA 94, 3320-3323, 1997). The primers used for amplification of this polymorphic site are 5'-TCCAGAACTCTGTTCCAGAGCGTGC-3' (forward primer) and 5'-GCTGTGAAGTTGCTGTTTCCTCAT-3' (reverse primer). These primers will be fluorescently labeled and the PCR product will be run on 310 genetic analyzer (Perkin Elmer Inc. Emeryville, CA) for accurate assessment of fragment length by automated fluorescence detection. Fluorescently labeled DNA markers will be used to construct a standard curve of peak arrival time. This standard curve will be used to calculate the CAG repeat length of the unknown DNA. The work will be done by Dr. Chilukauri Nageswararao (C.N. Rao) a member of the Center for Prostate Disease Research Team.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Analysis on the SRD582 gene has been completed. CYP384 gene has been optimized and studies will be initiated this year. Manuscript on SRD582 is in process.

#### CONCLUSIONS

None at this time.

WU# 2871-98 (05)

STATUS: O

TITLE: Involves collaboration with Dr. Anil Jaiswal - no subtitle given for this amendment

#### STUDY OBJECTIVE

A role of quinone oxidoreductases (NQ01 and NQ02) and transcription factor Nrf2 in prostate cancer is hypothesized because of the role these enzymes have in prevention of oxidative stress and neoplasia.

#### TECHNICAL APPROACH

Presently prostate cancer is defined as the prostate tissue biopsy positive for cancer cells as determined by the pathologist. Blood DNAs in cancer group come from patients who have undergone radical prostatectomy specimens and these individuals have clinically significant prostate cancers. A valid concern was raised that there may be prostate cancer predisposing genetic changes in some control individuals without clinical symptoms. At present we are faced with this limitation in prostate cancer field as no such genetic marker has been defined that has tight association with prostate cancer predisposition. In fact, the goals of this specific study to evaluate certain gene polymorphisms e.g., NQO1, NQO2 and Nrf2 that may be associated with increased risk of prostate cancer. Future implications of such studies are to define gene alterations that may have predisposing effects.

Exposure of cells to chemically induced oxidative stress is known to cause DNA and membrane damage, apoptotic cell death, degeneration of tissues, premature aging, mutagenicity and carcinogenicity. Accumulation of mutations in susceptible target tissue(s) due to oxidative stress is also suspected to play roles in age related cancers such as prostate cancer. NQO1 and NQO2 are cellular proteins that catalyze metabolic detoxification of chemicals (e.g. quinones and their derivatives) and protect the cells against oxidative stress [reviewed in V. Radjendirane, P. Joseph and Anil K. Jaiswal, Gene expression of DT-diaphorase (NQO1) in cancer cells. In "Oxidative Stress and Signal Transduction". Edited by Henry J. Forman and Enrique Cadenas. Publisher Chapman & Hall, New York. pp 441-475 (1997)]. This protection is due to prevention of superoxide formation. Nrf2 is a nuclear transcription factor that regulates the expression and induction of NQO1, NQO2 and other chemical detoxification enzymes. Since there is some evidence that oxidative stress may play a role in prostate cancer (W.H. Lee, R.A. Morton, J.I. Epstein, J.D. Brooks, P.A. Campbell, G.S. Bova, W.S. Hsieh, W.B. Isaacs and W.G. Nelson. Cytidine methylation of regulatory sequences near the pi-class glutathione S-transferase gene accompanies human prostatic carcinogenesis. Proc. Natl. Acad. Sci USA 91: 11733-11737, 1994), we plan to analyze NQO1, NQO2 and Nrf2 gene loci for germline polymorphisms/ mutations leading to the loss of decreased activity/expression of respective proteins. In the past, Dr. Anil Jaiswal's laboratory has cloned the genes encoding NQO1, NQO2 and Nrf2. They have all the necessary techniques and primers to amplify the various exons of these genes by PCR. The PCR amplified products will be analyzed by SSCP to detect mutations. The DNA samples detected with the mutations will be cloned and sequenced.

Dr. Anil Jaiswal in conjunction with the Center for Prostate Disease Research (CPDR) will analyze the polymorphism/ mutation of the above-mentioned genes in the constitutional DNAs (peripheral blood lymphocyte derived) of age matched individuals with or without prostate cancer. For this purpose we will use an aliquot of pre-existing DNA from 200 prostate cancer patients that we have utilized for our in house research projects. Additionally, we will need DNA from age matched 200 individuals without prostate cancer. These samples will come from the approved protocol WU# 2801 entitled "Establishment of a Serum Bank for Future Detection of New Prostate Cancer Markers in Serum of Patients with Prostate Cancer, Benign Prostate Conditions, and No Prostate Disease".

The polymorphisms/ mutations occurring at high frequency will be correlated with data on clinico-pathologic features of the cancer patients in a blinded fashion. In the related *in vitro* experiments, these mutations will be created in the respective proteins by site directed mutagenesis. The mutant NQO1 and NQO2 proteins will be analyzed for its capacity to detoxify chemicals. Similarly, the mutant Nrf2 proteins will be analyzed for its capacity to regulate the expression of genes encoding NQO1 and NQO2.

Human genes encoding NQO1, NQO2 and Nrf2 have been cloned and sequenced in Dr. Jaiswal's laboratory (Biochemistry 30: 10647-10653, 1991; JBC 269: 14502-14508, 1994; PNAS 91: 9926-9930, 1994). The primers have been synthesized to amplify the individual exons of these genes by PCR. PCR products will be analyzed by SSCP procedures established in Dr. Srivastava's laboratory (J. Urol 154:414,1995). Allelic variations will be detected by observation of difference in the mobility of DNA bands on the gels. The polymorphic variants will be subcloned in pcDNA3 vector (Invitrogen, California) and sequenced with T7 primer.

**In Vitro Experiments:** The specific allelic variants from PCR/SSCP/Sequencing results will be selected to determine if these polymorphisms/mutations result in the loss of the function of the respective proteins. We plan to use site directed mutagenesis kit from Invitrogen to incorporate specific mutations by procedures as described in the Manual from the manufacturer. The wild type and mutated cDNAs will be transfected in eukaryotic cells to overexpress the cDNA derived wild type and mutant proteins in separate experiments. The effect of site directed mutagenesis in

NQO1 and NQO2 proteins will be determined by NQO1 and NQO2 enzyme assays by procedures as previously described (JBC 263: 13572-13578, 1988; ABB 347: 221-228, 1997). The effect of mutations in Nrf2 will be determined by DNA-band shift assays by procedures as described (Oncogene 17: 3145-3156, 1998). These experiments will demonstrate that which of the specific mutations result in the loss of protein function.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

NAD(P)H: quinone oxidoreductase1 (NQO1) and NRH: quinone oxidoreductase2(NQO2) are flavoproteins that protect against chemically induced redox cycling, oxidative stress and neoplasia. The DNA samples from normal and prostate cancer patients were analyzed for mutations in Nrf2 gene that encodes for a nuclear factor important for NQO1 gene expression. No mutations in Nrf2 gene in either control or patient samples were detected. Current analysis is focused on identification of mutations in promoter elements that regulate expression of NQO1 gene.

#### CONCLUSIONS

None at the time.

WU# 2871-98 (07)

STATUS: O

TITLE: Novel Role of Candidate Tumor Suppressor Gene, ANX7 in Prostate Cancer

#### STUDY OBJECTIVE

Drs. Meera Srivastava's and Harvey Pollard's laboratory has discovered *ANX7* as a candidate tumor suppressor gene using *ANX7* gene knockout model (Srivastava et al., PNAS, 96, 13783-13788, 1999, see attached). Their studies hypothesize that *ANX7* gene alterations by loss of expression or mutations are important in human cancers. Therefore, *ANX7* expression will be analyzed in matched normal and tumor tissues of prostate cancer patients using laser capture dissection (LCM) and quantitative RT-PCR. *ANX7* expression will be correlated with clinico-pathologic features e.g.: pathologic stage of tumor, age, grade, size, and androgen receptor status and disease free survival after treatment. We will also analyze *ANX7* gene mutations using LOH and DNA sequence analysis.

Drs. Srivastava/ Pollard's laboratory has shown that reduced expression of the *ANX7* protein by semi-quantitative immunohistochemistry on tissue micro-arrays is significantly associated with prostate cancer progression. To further dissect if *ANX7* alteration is reflected at the transcription level, Drs. Srivastava and Pollard are proposing to collaborate with us to do a complementary study of *ANX7* expression at RNA level in human prostate cancer specimens available at CPDR. It is also possible that *ANX7* locus may have undergone deletions in tumors showing reduced or loss of *ANX7* expression. Therefore, DNA from prostate cancer specimens will also be analyzed for the loss of heterozygosity LOH, a common phenomenon associated tumor suppressor locus. Biologic activity of *ANX7* and *ANX7* knockout mice experiments strongly suggest that *ANX7* is a candidate tumor suppressor gene. Micro dissected normal and tumor specimens derived from radical prostatectomy of 50 prostate cancer patients will be utilized for expression of *ANX7* gene. We anticipate that about a third of specimens will show reduced or loss of *ANX7* expression. The experiments proposed here are complementary in nature to their previous immunohistochemistry studies and justify the sample size. These experiments may be extended to specific subset of cancer specimens depending on the preliminary data generated here.

#### TECHNICAL APPROACH

RNA from tumor and normal cells of individual patients will be isolated by laser capture micro-dissection (LCM) of the matched normal and tumor tissues. RNA will be prepared by the RNazol method. cDNA fragment representing the nucleotides 400-500 in the coding region of *ANX7* protein will be analyzed by TaqMan procedure using the Perkin Elmer-7700 machine. Analysis of the expression of GAPDH using similar procedure will serve as a control for the input RNA. Levels of *ANX7* in tissue specimens will be normalized with respect to GAPDH expression. Ratios of the *ANX7* expression between matched normal and tumor will be the final data for grouping specimens into reduced/loss of expression, elevated expression or no change. These data will be correlated to clinico-pathologic features of the tissue. LOH is a possible mechanism for reduction in *ANX7* expression in tumors. To test the hypothesis that loss of *ANX7* gene expression can result from loss of heterozygosity, we will use 4 pairs of microsatellite markers located on or near the *ANX7* locus. We have selected these on the basis of radiation hybrid screening of chromosome 10 (data not shown). PCR will be performed on the genomic DNA samples derived from



#### Work Unit # 2871-98 [Continued]

normal and tumor specimens. PCR products will be analyzed on Perkin Elmer 300 DNA Analyzer. LOH will be scored using the built in software in 310 DNA analyzer.

The data on *ANX7* expression or *ANX7* deletions will be correlated with various clinico-pathologic features and their statistical significance will be determined using univariate and multivariate analyses. The statistician with CPDR will perform these analyses.

The proposed experiments will be done in collaboration with Dr. Shiv Srivastava group at CPDR. PCRs will be performed by Drs. Meera Srivastava and Harvey Pollard group in the Department of Anatomy and Cell Biology at USUHS. TaqMan and LOH assays will be performed at CPDR laboratory by a postdoctoral fellow from Drs. Meera Srivastava/Harvey Pollard group. To assist CPDR in this project we also want to add Dr. Meera Srivastava, Ph.D. and Dr. Harvey Pollard as collaborating personnel.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Using the metastatic androgen insensitive DU145 prostate cancer cells as model system, we observed that over expression of *ANX7* caused the cancer cells to undergo apoptosis. Introduction of adenovirus wild-type *ANX7* in nude mice suppresses tumor formation by 100% in vivo. The crucial signaling components involved in tumor suppression and apoptosis induced by *ANX7* in prostate cancer cells were identified using human cancer cDNA microarray. We found a six-fold elevation in cyclin E2 level. Indeed, the cells were arrested at S phase with a huge percentage of cells accumulated at S phase.

#### CONCLUSIONS

Therefore, we conclude that the *ANX7* gene kills prostate cancer cells by increasing cyclin E2 levels, thereby accumulating cells at S phase and arresting cells at S phase causing apoptosis. In addition, high levels of *ANX7* in breast tumor correlate strongly with poor survival of HER2 negative patients and most aggressive forms of breast cancer. This is the first study to demonstrate that *ANX7* antibody has the potential for development into an in vivo diagnostic and therapeutic tool.

WU# 2871-98 (09

STATUS: C

TITLE: Evaluation of Glutamine Repeat Protein-1 (GRP-1) Expression in Prostate Cancer

#### STUDY OBJECTIVE

Glutamine repeat Protein-1 (GRP-1) is expressed most abundantly in mouse testis, expressed differentially in rat prostate tissues, and expressed in several human prostate cancer cell lines. As part of a project aimed at examining the role of GRP-1 in the regulation of androgen receptor activity and prostate cancer, we propose (1) to examine the expression of GRP-1 in benign and malignant human prostate tissues and (2) to analyze benign and malignant human prostate tissues for mutated GRP-1. Our working hypotheses are that GRP-1 expression is regulated by androgen and that there is an alteration of GRP-1 expression and/or function in the prostate that coincides with progression from benign to malignant tissue. Overall, we suggest that decreased expression or function of GRP-1 (or GRP-1-interacting proteins) plays a role in the progression of prostate cancer to androgen-independence. The major rationales for doing the work proposed are that (1) GRP-1 is expressed predominantly in androgen-responsive tissues and may be regulated by the androgen signaling pathway and (2) GRP-1 represses androgen receptor activity and alteration of GRP-1's expression and/or function (including that due to polymorphism of the polyglutamine/glutamine-rich region) may be associated causally with the progression of prostate cancer.

#### TECHNICAL APPROACH

Briefly, RNA from normal and tumor tissues (40 total RNA specimens; 20 each of normal and malignant prostate) will be analyzed for GRP-1 gene expression by quantitative reverse transcriptase-polymerase chain reaction analyses using the TaqMan procedure and ABI Prizm 7700 sequence detection system (PE Biosystems, Inc. documentation and protocols). The housekeeping genes GAPDH and epithelial cell-specific cytokeratin 18 will be analyzed simultaneously as controls. We will also examine DNA from the same benign and malignant human prostate tissues for expansion or deletion polymorphism within the polyglutamine/glutamine-rich domain of GRP-1. Genomic

Work Unit # 2871-98 [*Continued*]

DNAs will be subjected to PCR amplification using GRP-1-specific primers that flank the histidine-glutamine-glutamine- and polyglutamine-rich domain (i.e., bp 280-624). Labeled PCR products will be resolved by electrophoresis in 3.5% native polyacrylamide gels and analyzed by automated DNA sequencing.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Funding was not granted. Project is closed with no work done.

CONCLUSIONS

Not available.

WU# 2871-98 (10)

STATUS: C

TITLE: Expression of 1D10 Antigen in Prostate Cancer

STUDY OBJECTIVE

We propose to do an initial screening of 1D10 antigen in prostate cancer. The Walter Reed group has demonstrated that patients with more aggressive CLL (i.e. those requiring significant numbers of treatment cycles for their disease or being refractory to fludarabine) have a higher frequency of being negative for this antigen. We will examine expression in three different grades of prostate cancer (well differentiated, moderately differentiated, and poorly differentiated). We will examine a total of 12-15 patients in each group as an initial pilot study.

The primary objective of this pilot study is to prove the null hypothesis that being that 1D10 positively occurs at a frequency below 26% in each of these subsets. Such a low frequency of expression would make further exploration of this antibody in prostate cancer of little interest. The 95% confidence interval is 0-26% if zero of ten evaluable patients are positive for this antigen. It may be anticipated that 2-5 samples may not be adequate for staining. Therefore, we will examine 12-15 samples from each group and effectively prove the null hypotheses if no patients in this group are positive for 1D10 antigen expression.

TECHNICAL APPROACH

The expression of 1D10 antigen on tumor tissues will be tested using the immunohistochemistry assay using standard methodology. This requires frozen sections from prostate tumors bearing the histology documented above. If any additional extra samples are not used they will be discarded at PDL. PDL will perform this immunohistochemical staining. The assay employed by PDL has been validated as part of the ongoing NHL phase I trial in which Walter Reed Army Medical Center is participating. To assist CPDR in this project, we also want to add Dr. Joseph M. Flynn as collaborating personnel.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The investigator responsible for the work under this amendment has left. No additional work has been completed since the last APR and this project has been closed.

CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: Macroscopic and Microscopic Anatomy of the Arterial Supply to the Human Vas Deferens

KEYWORDS: arterial supply, vas deferens, cadaver

PRINCIPAL INVESTIGATOR: Dean, Robert LTC MC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: O

SERVICE: Urology

INITIAL APPROVAL DATE: 11 August 1998

### STUDY OBJECTIVE

The objective is to describe the gross and microscopic blood supply to the vas deferens. Additional objectives are to assess the variability of the arterial and venous structures, assess collateral blood supply to the vas deferens, and to utilize the new understanding of the vascular supply to improve operations on the spermatic cord, scrotal adnexa and vas deferens.

### TECHNICAL APPROACH

The gross dissection of the deferential blood supply will be to perform gross dissection of cadaveric and autopsy specimens, dissection of en bloc spermatic cord specimens from formalin preserved and frozen cadavers, and microdissections on cadaveric specimens and autopsy specimens and recording of findings using photos and drawings. The microscopic description of deferential blood supply will include injection studies and will be performed using methylene blue injections of the deferential artery, internal iliac artery and internal spermatic artery. Specimens will also be injected with resin, and the surrounding soft tissue treated with acidifying agent to create casts of the deferential artery and its branches. Histologic sections will be performed using a dissecting microscope in the straight and convoluted portions of the vas deferens sagittally and transversely. These sections will be recorded using photomicrographs and drawings from medical illustrators. The donated cadavers/autopsy specimens will be provided by USUHS. The dissection will be conducted in the Anatomical Teaching Laboratory at USUHS.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are no new literature findings to report. No amendments or modifications to the research study have been made since the last review. No adverse events have occurred and no patients have withdrawn from the study. The PI for this protocol has been deployed since February 2003.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

### CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: Study of the Safety and Effectiveness of the Mentor Saline-Filled Testicular Prosthesis

KEYWORDS: prosthesis, testicular, implant

PRINCIPAL INVESTIGATOR: McLeod, David G. COL MC

ASSOCIATES: Peppas, Dennis S. LTC MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: Urology

INITIAL APPROVAL DATE: 1 September 1998

### STUDY OBJECTIVE

The objectives of the study are to assess the safety and effectiveness of the Mentor saline-filled testicular prosthesis. We will also look at the rates of and time to explantation, revision and other re-surgery of the prosthesis.

### TECHNICAL APPROACH

This is a multi-center open label study. Patients are stratified into four groups: adult males who are missing their testicle at baseline; adult males who are not missing their testicle at baseline; pediatric males who are missing their testicles at baseline and pediatric males who are not missing their testicle at baseline. Patients will be followed for five years. Patients complete quality of life questionnaires and satisfaction questionnaires throughout the length of the study

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This is a multi-center study with 18 sites involved. To date, 10 patients have been enrolled in this study at WRAMC. Since last APR, 0 patients have been enrolled at WRAMC. The total number of subjects enrolled study-wide is 149. Enrollment ended August 31, 1999. A total of 9 patients have received the testicular prosthesis at WRAMC. Patient 007 was sent TDY out of the country prior to surgery and dropped from the study. Patient 002 has had his prosthesis explanted due to its placement and migration and is withdrawn from the study. Patient 004 transferred to Korea and is lost to follow-up. Patient 006, 008 and 010 have moved without a forwarding address and are not able to be located. They are lost to follow-up. Patients 003 and 005 have moved and are unable to remain in the study. All adverse events occurring at WRAMC have been reported. No serious adverse events have been reported from other sites.

### CONCLUSIONS

The Food and Drug Administration has approved Mentor's Pre-Market Approval application. The FDA has determined the device to be safe and effective in terms of low rates of adverse events, restoring a normal appearance to a male's genitalia, and psychological benefits. The device has been released for market in the United States. The approval was granted on clinical data submitted through one year of follow-up and remains contingent on collecting data out to five years.

## DETAIL SUMMARY SHEET

TITLE: Retrospective Study of the CPDR Prostate Cancer Database to Perform Statistical Modeling Using Pre-Treatment Prognostic Variables in Predicting Disease Progression After Radiotherapy for Clinically Localized Prostate Cancer

KEYWORDS: statistical modeling, disease progression, prostate cancer

PRINCIPAL INVESTIGATOR: Moul, Judd W. COL MC

ASSOCIATES: Petroski, Raymond CPT MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: Urology

INITIAL APPROVAL DATE: 29 October 1998

### STUDY OBJECTIVE

1) To use pre-treatment prognostic variables to predict disease progression in men who have received primary external beam radiotherapy (XRT) using regression analysis 2) Validate a regression equation to predict disease recurrence in men who have received primary external beam radiotherapy in localized prostate cancer

### TECHNICAL APPROACH

Retrospective chart review using the CPDR database WU#2857 of all men treated with XRT at WRAMC between 01 January 1989-30 June 1996. The Cox proportional hazards model will be used to assess the simultaneous influence of possible predictor variables on time to disease recurrence after treatment with XRT. Patients will be placed into age, race and stage matched cohorts, with 70% of the patients being used to create the model and the remaining 30% used to validate the model. A backward stepwise elimination procedure will be used to remove the covariates from the model if they are not correlated to the risk of recurrence.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are no new literature findings to report.

There have been no adverse events.

This is still in progress and has not been completed because of resident graduation and lack of Radiation Oncology support due to multiple Radiation Oncologists leaving active duty at Walter Reed. We have now identified a Navy Radiation Oncologist (Dr. Robert Douglas) who will collaborate and we plan to complete this protocol in the coming year.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is N/A, if multi-site study.

### CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: Cyclosporine Treatment and the Effect on Post Vasovasostomy Semen Parameters in the Lewis Rat

KEYWORDS: vasectomy, anti-sperm antibodies

PRINCIPAL INVESTIGATOR: COL Dennis Peppas, MC  
ASSOCIATES:

DEPARTMENT: :Surgery  
SERVICE: Urology

STATUS: C  
INITIAL APPROVAL DATE: 3 November 1998

### STUDY OBJECTIVE

The study objective is to study the effect of cyclosporine therapy on semen parameters after vasovasotomy and the correlation between semen parameters and levels of antisperm antibodies.

The hypothesis is that the use of cyclosporine in conjunction with Vasovasostomy will improve semen parameters in previously vasectomized rat. This will be directly correlated with decrease in antisperm antibodies in cyclosporine treated rats.

### TECHNICAL APPROACH

Using Lewis rats we will create individual groups to include treated and untreated rats with cyclosporine. These groups will initially undergo vasectomy and then vasovasotomy with pre and post semen analysis to determine improved semen parameters in the treated groups. These parameters will be correlated with pre and post antisperm serologic and semen antibodies. A control group of nonvasectomized rats will be used to determine baseline antisperm antibodies and normal semen parameters. These groups will consist of approximately ten animals. Cyclosporine will be dose at 10mg/kg in the treated groups.

### PRIOR AND CURRENT PROGRESS

Data acquisition is complete. Statistical analysis is complete. Scientific paper is nearing completion.

### CONCLUSIONS

Pending the completion and publication of the paper.

## DETAIL SUMMARY SHEET

TITLE: ALZA Overactive Bladder Registry Design Document

KEYWORDS: overactive bladder, incontinence

PRINCIPAL INVESTIGATOR: Dean, Robert C. LTC MC

ASSOCIATES: Michael J. Danier CAPT MC USN

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: O

INITIAL APPROVAL DATE: 08 June 1999

### STUDY OBJECTIVE

The principle objective of this study is to provide comparative outcome information on the effectiveness, tolerability, and quality of life associated with different types of treatments, both pharmacological and behavioral for overactive bladder. The secondary objectives of this study are to: estimate resource utilization of health care services attributable to overactive bladder, provide physician-specific information to enhance patient care, and identify areas for possible further study.

### TECHNICAL APPROACH

Patients were enrolled from the urology clinic. Patients with a newly diagnosed overactive bladder or patients with overactive bladder that have been off medication for at least 12 months were asked to participate. Patients completed the required diaries and questionnaires and will be followed up via telephone calls from the Overactive Bladder Registry at 3 months, 6 months and then every 6 months until up to 3 years. Patients may withdraw at any time.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search has been done and there are no new findings to report. No adverse events have occurred.

Enrollment for the pilot portion of the program was completed and the patients are finishing up the follow-up portion of the data collection.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 15. The total number enrolled study-wide is 217, if multi-site study.

### CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: Radical Prostatectomy of Prostate Cancer Patients and Circulating Cancer Cell Test (CCCT)

KEYWORDS: Circulating, Cancer cell, Prostate

PRINCIPAL INVESTIGATOR: Moul, Judd COL MC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: O

SERVICE: Urology

INITIAL APPROVAL DATE: 27 July 1999

### STUDY OBJECTIVE

To use the CCCT to determine the incidence of circulating prostate cancer cells: 1) before, during, and after radical prostatectomy (RRP) and correlate the positive detection of circulating cancer cells to disease recurrence after surgery, and 2) to correlate the relationship of CCCT and RRP surgical path findings.

### TECHNICAL APPROACH

CCCT is drawn within ten days of RRP, within ten minutes after the prostate is removed, on discharge from WRAMC and 3-4 weeks after the surgery. These patients are followed every six months for five years.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature review has been done and there are no new results to report.

The number of subjects enrolled to the study since last APR at WRAMC is 25 and the total enrolled to date at WRAMC is 48. No serious or adverse events have occurred at WRAMC or been reported by the sponsor. Forty-four (44) subjects are actively participating in the study. Three (3) subjects have voluntarily withdrawn from the study and one (1) subject has left the area, not able to be contacted, and is lost to follow-up.

### CONCLUSIONS

None at this time.



## DETAIL SUMMARY SHEET

TITLE: Creation of a Prospective and Retrospective Database of Patients Evaluated and Treated for Urinary Incontinence

KEYWORDS: database, incontinence, therapy

PRINCIPAL INVESTIGATOR: Dean, Robert LTC MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: O  
INITIAL APPROVAL DATE: 11 August 1998

### STUDY OBJECTIVE

To collect retrospective and prospective data beginning 1 May, 1994 on all patients age 18 years or older, who present to the Urology and Urogynecology Clinics at Walter Reed Army Medical Center (WRAMC) with the complaint of urinary incontinence. To use this database to analyze treatment outcomes for patients undergoing therapy for urinary incontinence. Analysis will include, but not be limited to: risk of development of urinary incontinence; risk of recurrent incontinence; therapy failure; therapy durability; complications of therapy; efficacy of therapy based on type of incontinence; and comparison of therapy modalities.

### TECHNICAL APPROACH

To prospectively and retrospectively collect data on patients seen in the Urology and Urogynecology Clinics at WRAMC complaining of urinary incontinence. Information collected will be those data points included on Database Forms. The procedures and tests in this protocol are standard of care for urinary incontinence. Separate consent forms will be obtained for the standard of care testing and procedures. The only thing that is not standard of care is the questionnaires. Patients participating in the study will be given additional questionnaires to complete. The history, physical examination, and testing will be the same for the patients that participate on this study as it would for patients that do not participate on this study. All patients will undergo complete history and physical based on gender, American Urological Association symptom score questionnaire, urodynamics study, quality of life questionnaire, three day voiding diary, one hour pad test, and sexual function questionnaire. Patients will then be offered therapy based on current practice. Patients will undergo repeat evaluation (the same type of an evaluation as the initial evaluation), 6 month, 1 year following onset of any therapy received. In addition to the initial and the 6 months to one-year evaluations any additional follow ups, examinations or tests, pertaining to incontinence, required throughout patient's treatment would be recorded.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are no new literature findings to report. No amendments or modifications to the research study have been made since the last review. No adverse events have occurred and no patients have withdrawn from the study. The PI for this protocol has been deployed since February 2003 and there have been continued computer problems.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is N/A, if multi-site study.

### CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: #VCL 1102-203 - Phase II Study Evaluating the Safety and Efficacy of Neoadjuvant Leuvectin Immunotherapy for the Treatment of Prostate Cancer (and Amendment 1)

KEYWORDS: prostate, cancer, immunotherapy

PRINCIPAL INVESTIGATOR: Moul, Judd COL MC

ASSOCIATES: McLeod, David COL MC; Esther, Thomas PA; Gallagher, Jane RN BSN

DEPARTMENT: Surgery

STATUS: O

SERVICE: Urology

INITIAL APPROVAL DATE: 31 August 1999  
(Six-month review)

### STUDY OBJECTIVE

Further investigate the toxicity and tolerability of Leuvectin in this patient population. Collect a database of PSA values, slope over time, and clinical assessment to estimate the effect of Leuvectin in preventing or delaying manifestations of prostate cancer progression.

### TECHNICAL APPROACH

This is an open label, multicenter study of patients with evidence of locally recurring prostate cancer following radiation therapy. Patients will receive up to three series of 2 intraprostatic injections of Leuvectin followed by one year of follow-up visits every three months with no additional treatment. An amendment (#1.02) was submitted and reviewed at the 6/21/00 HUC Meeting which changed the inclusion criteria to lower the PSA value from 10ng/ml over a 6 month period to > 1.0ng/ml over a 3 month period to adhere more closely with the standard of care. An amendment (#1.03) was submitted and reviewed at the 6/21/00 HUC Meeting that changed the exclusion criteria to include patients who have had neoadjuvant hormonal therapy prior to radiation therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study was closed for enrollment in 11/01. The total number of patients enrolled in this study since last APR is 0 and the total enrolled to date at WRAMC is 4. Of the four (4) patients enrolled at WRAMC, two (2) have withdrawn from the study due to disease progression with rising PSA and have started on second line therapy, and two (2) continue to be followed per protocol. Twenty-three (23) patients were enrolled study-wide. No new adverse events have occurred at WRAMC or any other site.

### CONCLUSIONS

None to date.

## DETAIL SUMMARY SHEET

TITLE: #VCL 1102-203 - Phase II Study Evaluating the Safety and Efficacy of Neoadjuvant Leuvectin Immunotherapy for the Treatment of Prostate Cancer (and Amendment 1)

KEYWORDS: prostate, cancer, immunotherapy

PRINCIPAL INVESTIGATOR: Moul, Judd COL MC

ASSOCIATES: McLeod, David COL MC; Esther, Thomas PA; Gallagher, Jane RN BSN

DEPARTMENT: Surgery

STATUS: O

SERVICE: Urology

INITIAL APPROVAL DATE: 31 August 1999  
(Six-month review)

### STUDY OBJECTIVE

Further investigate the toxicity and tolerability of Leuvectin in this patient population. Collect a database of PSA values, slope over time, and clinical assessment to estimate the effect of Leuvectin in preventing or delaying manifestations of prostate cancer progression.

### TECHNICAL APPROACH

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### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study was closed for enrolment in November of 2001. The total number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 4. Of the four (4) patients enrolled at WRAMC, two (2) have withdrawn from the study due to disease progression with rising PSA and have started on second line therapy, and two (2) have been discontinued on study due to sponsor initiated protocol amendment, and are being followed in the clinic for long term care. The total number enrolled study-wide is 23, if multi-site study. No serious or adverse events have occurred at WRAMC or been reported by the sponsor.

### CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: Database of Urinary Stone Patients

KEYWORDS: database, kidney stone, outcomes

PRINCIPAL INVESTIGATOR: Schenkman, Noah LTC MC

ASSOCIATES: Spevak, Marianne CCRC

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: O

INITIAL APPROVAL DATE: 07 September 1999

### STUDY OBJECTIVE

The goals of this study are to accumulate long-term data on all kidney stone formers in our clinic. This information will be used to provide needed epidemiologic information on urolithiasis. The information provided will answer questions such as the impact of kidney stones on military readiness, effectiveness of medical treatment regimens and the true recurrence rate of kidney stones in the modern era. With the exception of the completion of patient questionnaires, all other testing, procedures, and patient history are standard of care.

### TECHNICAL APPROACH

Male and female patients with confirmed urinary stone disease by either radiographic imaging or passage of calculi will be included in this study. Patients that do not have confirmed stone disease by either of those two methods will be excluded. A clinical suspicion of stone disease does not warrant inclusion - it must be confirmed urinary stone disease. After the diagnosis of urolithiasis is made, the patients will be given information about the database. The patients will then be asked to sign an informed consent if they wish to participate. An initial evaluation will include a complete history and focused physical examination. The patient will be asked to fill out the stone database questionnaire. The following results will be recorded, if available: initial laboratory work including serum electrolytes, uric acid, calcium, phosphorus and parathyroid hormone; stone analysis; and radiographic and imaging exams; twenty-four hour urine analysis. The patient's clinical course and condition will dictate follow up. Data of each follow-up, including surgical procedures, will be recorded. There have been no modifications to date.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

We continue to accumulate data for this study and enrollment is ongoing. We are still working out details of getting automatic downloads of the lab studies into the database to greatly facilitate operations. At present, we have not analyzed any data. There have been no new studies in the literature that will influence this study.

The number of subjects enrolled to the study since last APR at WRAMC is 170 and the total enrolled to date at WRAMC is 267. The total number enrolled study-wide is 267, if multi-site study.

### CONCLUSIONS

N/A

## DETAIL SUMMARY SHEET

TITLE: Characterization of the Cytokines Mediating Different Phases of Inflammation Following Controlled Head Trauma

KEYWORDS: cytokines, transphenoidal hypophysectomy, temporal lobectomy

PRINCIPAL INVESTIGATOR: Popa, Christian MAJ MC

ASSOCIATES: Calkins, Mark MAJ MC; Ling, Geoffrey LTC MC; Blanchard, Jeremy, MAJ MC; Fitzpatrick, Thomas COL MC

DEPARTMENT: Surgery

STATUS: C

SERVICE: Critical Care Medicine

INITIAL APPROVAL DATE: 27 October 1998

### STUDY OBJECTIVE

To characterize the serum and cerebrospinal fluid level of several inflammatory Cytokines at serial time points following controlled head trauma. We hypothesize that both pro-inflammatory and anti-inflammatory cytokines are released.

### TECHNICAL APPROACH

Transphenoidal hypophysectomy patients, acoustic neuroma surgery patients, and patients undergoing temporal lobectomy for refractory seizures will serve as controls and surgical models of head trauma respectively. There have been no addenda to this protocol.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

We have previously enrolled and collected data on a total of 4 subjects, all of who underwent transphenoidal hypophysectomy with lumbar drain placement. These four patients did well, and there were no study-related adverse effects. We have analyzed this data for TNF-a, IL-1, and IL-6 by chemiluminescence, and noted a rise in CSF TNF-a, as well as a bimodal elevation of CSF IL-6, which was mirrored by a smaller rise in blood IL-6.

We have tried unsuccessfully to recruit additional patients within the last year in order to publish a case series. We are therefore closing this protocol. There have not been any significant developments, findings or publications that would warrant modification of the protocol.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 3. The total number enrolled study-wide is N/A, if multi-site study.

### CONCLUSIONS

Closed for insufficient enrollment.

## DETAIL SUMMARY SHEET

TITLE: Survey of Prevalent Pollen and Fungal Aeroallergens in the Washington DC Area

KEYWORDS: pollen, aeroallergen, fungal

PRINCIPAL INVESTIGATOR: Kosisky, Susan

DEPARTMENT: Allergy-Immunology

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 11 May 1993

### STUDY OBJECTIVE

To identify the predominant aeroallergens in the Washington, DC area. Identification of prevalent trees, weeds, and grasses are essential to the effective treatment and diagnosis of the allergic patient. Daily volumetric samples will reveal peak concentrations and pollination periods for area allergenic aeroallergens. Seasonal definition of pollination periods for trees, weeds, grasses, and molds will allow for the development of a better patient treatment regimen.

### TECHNICAL APPROACH

Daily volumetric sampling using a Rotorod Sampler is conducted. Two polyurethane "I" rods are exposed to the atmosphere for collection of aeroallergens. I rods are coated with a Silicone Grease adhesive for particle collection. The rods are microscopically examined for pollen grains and mold spores. Counts are converted to a volumetric grains/cubic meter assessment.

\*Modification - The Rotorod Sampler is located on the roof of Building 512 at Forest Glen, Silver Spring, Maryland. Counts are conducted daily, weather permitting. \*Modification - Addition of a Burkhard Spore Trap Sampler that has been added to sample more effectively the smaller mold spores (spores less than 10-15 microns in size). The Burkhard sampling device involves using a slide coated with Silicone Grease that is exposed to the atmosphere for 24-hour collection periods. Air is drawn into the Burkhard Spore Trap Sampling Chamber through an orifice depositing the spores on the coated slide surface. The slide is then examined microscopically for mold spores. Counts are conducted daily weather permitting. The Spore Trap is located on the roof of Bldg 512, Forest Glen, Silver Spring, MD.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The pollen and spore reports continue to be submitted to the National Allergy Bureau for public dissemination. As of March 2003 the American Academy of Allergy, Asthma and Immunology's National Allergy Bureau has developed a new website to improve the aeroallergen reporting process to include better access to media outlets nationwide. Local Channel TV 9 (WUSA) has incorporated our aerobiological data into their Washington, DC news website. Reports are sent to CNN, Channel 4 news and WTOP for media releases of aerobiological information. A public information group for the daily pollen and mold spore reports continues to serve the Walter Reed Community and DOD Region 1 through Outlook and various local websites. Data and photos of pollen, spores and allergenic plants continue to be published through the Academy of Allergy, Asthma and Immunology's Pollen and Spore Report and other informative pamphlets and handouts. The analysis of pollen and spore data continues as well as the correlation with meteorological variables. Our aerobiological center for the Washington, DC area continues to support area allergists by providing data used for various study protocols.

### CONCLUSIONS

This study is ongoing and continues to provide daily aerobiological data to local and national media organizations, the National Allergy Bureau (AAAAI) and numerous websites that assist in effectively disseminating the information for public and scientific concerns. Continued data collection over time allows for us to establish trends with respect to the seasonal distribution and prevalence of predominant area allergenic offenders. Year to year

Work Unit # 3369 [*Continued*]

variations occur with respect to seasonal concentrations. Interestingly, in the same season, while some tree species had heavy pollen production other trees had a low production year. Biennial or cyclic patterns to pollen production are currently being assessed as part of this study. To date such patterns are not clearly evident. Continued data analysis will also allow for better establishing correlations with meteorological variables to provide for a predictive model. The data has also been used to develop a standardized skin test panel to be employed in the DOD Region 1 area as well as nationwide. Data on aeroallergen prevalence continues to offer insight into predominant regional aeroallergens. This has assisted in refining our inventory of aeroallergen vaccines to be used for testing and treatment of the atopic patient. A reduction has resulted in savings in time and money. Various aeroallergen manufacturers continue to use our data to supply extracts of predominant molds and pollens for testing and treatment of the atopic patient.

## DETAIL SUMMARY SHEET

TITLE: Mosquito Hypersensitivity: Immunology and Value of Skin Testing with Whole Body Mosquito Extracts

KEYWORDS: skin testing, mosquito, hypersensitivity

PRINCIPAL INVESTIGATOR: Engler, Renata COL MC  
ASSOCIATES:

DEPARTMENT: Allergy-Immunology  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 21 December 1993

### STUDY OBJECTIVE

To: 1) determine the sensitivity, specificity and predicative value of prick and intradermal skin tests at different dilutions to mosquito whole body extracts; 2) measure the total mosquito-specific IgE and IgG and IgG subclasses in patients with no reactions, minor reactions, large local reactions, and systemic anaphylaxis to mosquito bites.

### TECHNICAL APPROACH

A total of 60 clinically negative subjects (with no adverse reactions to mosquito bites) and 60 clinically positive subjects will be enrolled. Prick and intradermal skin tests with *Aedes aegypti* and *Culex pipiens* mosquito extracts in five dilutions will be administered. A permanent imprint of the wheal and flare will be measured. Blood will be drawn before and 3 weeks after skin testing to evaluate mosquito-specific IgG, IgG subclasses, and IgE.

### PRIOR AND CURRENT PROGRESS

A total of 36 subjects have been enrolled since the study began. Only five subjects have had positive reactions and thirty-one have had negative reactions. The adverse reactions were neither serious nor unexpected. Due to the small number of people who have this hypersensitivity, we have not seen any new mosquito bite anaphylaxis cases this year. As a result, no further subjects have been enrolled. Nevertheless, we would like to keep this protocol open so that subjects can be enrolled as they present. The subjects may not personally benefit from the study, but the medical community will gain an enhanced knowledge of the efficacy of prick and intradermal skin testing to treat mosquito bite anaphylaxis.

### CONCLUSIONS

No strong correlation has been shown between dilution strength of whole body extracts and reaction history of the subjects enrolled in this study.



## DETAIL SUMMARY SHEET

TITLE: Adverse Reactions with Intravenous Immunoglobulin Therapy

KEYWORDS: adverse reactions, intravenous immunoglobulin

PRINCIPAL INVESTIGATOR: Engler, Renata COL MC  
ASSOCIATES:

DEPARTMENT: Allergy-Immunology  
SERVICE:

STATUS: C  
INITIAL APPROVAL DATE: 10 December 1996

### STUDY OBJECTIVE

To review, retrospectively and prospectively the quality assurance monitor data collected for the IVIG subcommittee of the WRAMC Pharmacy and Therapeutics Committee. To determine the incidence and demographics of adverse reactions to IVIG between 1991 and 1995 using the CHCS pharmacy register of administrations, laboratory clinical results and individual patient chart reviews. To monitor, prospectively the adverse reactions associated with both intra muscular and IVIG therapy at WRAMC and to develop a database registry. To establish a serum bank and to determine if proteinuria is a "normal" side effect of IVIG therapy.

### TECHNICAL APPROACH

The Department of Allergy and Immunology provides all adult immunizations including IVIG therapy. A database of immunizations exists back to 1992 so that subjects have received IVIG therapy can be identified. The actual work of this protocol includes: monthly monitoring of patients receiving IVIG, entering adverse reactions into database, tabulating QA questionnaires from IVIG patients, monthly reviews of IVIG doses and volumes given establishment of a serum bank of patients receiving IVIG and gammaglobulin used at WRAMC, quantifying the level of proteinuria and microhematuria associated with the administration of IVIG by urine dipstick test before and after IVIG. A patient questionnaire filled out at the time of IVIG administration will be kept on file at the Allergy Clinic.

### PRIOR AND CURRENT PROGRESS

Since the AI clinic provides IVIG therapy for all the adults at WRAMC, we have access to potential research subjects for prospective enrollment. The WRAMC pharmacy is also providing additional subjects for prospective enrollment, and a means of retrospectively identifying prior adverse effects. Although the IVIG workload has decreased within the last year, sixteen enrollees have been maintained who are actively participating in this research. No one has dropped out, but our enrollment has not increased. This study is designed to observe adverse reactions during clinically indicated immunoglobulin administration. Immunoglobulin is not administered based on study participation. No adverse reactions have occurred as a result of study enrollment.

### CONCLUSIONS

The expected completion time for data analysis is the middle of FY 2003. No common adverse reaction has been correlated with the IVIG therapy.

## DETAIL SUMMARY SHEET

**TITLE:** A Phase 3 Study to Determine the Efficacy and Safety of C1-Inhibitor (HUMAN) Vapor Heated Immuno in Subjects of Hereditary Angioedema (HAE)

**KEYWORDS:** Hereditary Angioedema, C1-Inhibitor

**PRINCIPAL INVESTIGATOR:** Nelson, Michael LTC MC

**DEPARTMENT:** Allergy-Immunology  
**SERVICE:**

**STATUS:** C  
**INITIAL APPROVAL DATE:** 25 May 1999

**STUDY OBJECTIVE** The purpose of this study is to provide effective documentation to support an application to the Food and Drug Administration for the C1-Inhibitor (HUMAN) drug to be licensed in the United States to treat Hereditary Angioedema (HAE). This drug is in the final stage of testing. This drug will be given to a large number of patients (adults, children and pregnant adults) to find out its safety and effectiveness. HAE is caused by a lack of an adequate amount of a blood substance called C 1-Inhibitor. C1 concentrates can be made from human blood to replace this missing substance. This kind of therapy may reduce the swelling associated with attacks of HAE, as well as the associated pain and discomfort.

**TECHNICAL APPROACH** This study is divided into 4 parts: In part 1, the-patients will receive two treatments for an acute attack of HAE. They will be randomly assigned to treatment with either C1-Inhibitor or placebo. At one hour from the beginning of their first treatment, they will receive the other product (i.e., if the patient receives C1-Inhibitor first, the placebo will be received second; if the patient receives the placebo first, the C 1-Inhibitor will be received second). The doctor will not know whether the patients will be receiving C1-Inhibitor or the placebo. However, if needed, the doctor can find out from the pharmacy which treatment the patients will be receiving. In part 2, the patients will receive open label active C1-Inhibitor (HUMAN) for acute attacks of HAE. In part 3, the patients will receive active CI-Inhibitor (HUMAN) to prevent an attack should they require surgery. In part 4, females who are pregnant will be able to receive active C1 -Inhibitor (HUMAN) under a separate consent form. Part 1 of the study was completed and the results reported to investigators on 23 March 2002. Enrolled subjects will enter part 2 or 3 without the need to complete part 1. Parts 2, 3, and 4 will continue until licensure of the product or close of the study. An addendum to the protocol dated 4 January 2001 increased the number of enrollees allowed nationwide to 200.

**PRIOR AND CURRENT PROGRESS** The intermediate results discussed with investigators on 23 March 2002, and summarized in 26-27 March 2002 communications, are summarized as follows:

- 60 patients treated under part 1 (randomized)
- 15/60 reported relief within one hour (8 treated with experimental drug, 7 with placebo).
- Study failed to show a difference between the C1-Inhibitor group and the placebo group (p=0.766)
- 350 HAE attacks under part 2 (open label).
- 260/350 abated within one hour (81%)
- The Food and Drug Administration has been made aware of these results and Baxter will not receive licensure for the plasma-derived C1 Inhibitor (HUMAN) in the United States.
- No safety concerns elaborated.
- The protocol will continue through 30 September 2002, and restricted to enrolled patients under parts 2, 3, & 4.
- Another manufacturer is attempting to initiate a related protocol in the future.
- Compassionate use of product upon request will not be permitted by manufacturere.
- Enrollment remains closed.

**WRAMC update**

- One serious adverse event, most likely unrelated to study drug, resulted in death of subject # 13-001.
- Close-out site visit by Parexel monitor 15 January 2003.

**CONCLUSIONS** No further conclusions.

## DETAIL SUMMARY SHEET

TITLE: Lymphocyte Signaling Defects in Patients with Lupus

KEYWORDS: autoimmunity, cell signaling, immune cells, humans

PRINCIPAL INVESTIGATOR: Tsokos, Gregory COL MC

ASSOCIATES:

DEPARTMENT: Medicine

SERVICE: Rheumatology

STATUS: C

INITIAL APPROVAL DATE: 21 July 1998

### STUDY OBJECTIVE

Characterize signaling abnormalities in human autoimmune cells. Specifically, study the antigen-mediated signaling events including activation of kinases, phosphatases, calcium mobilization and transcription factor activation in lymphocytes from patients with systemic autoimmune diseases (lupus).

### TECHNICAL APPROACH

Isolate lymphocytes from peripheral blood; perform calcium mobilization studies; measure kinase and phosphatase activity using biochemical assays, measure transcription factor activity using shift assays.

### PRIOR AND CURRENT PROGRESS

We established the overall prevalence of zeta chain deficiency in patients with SLE. We found that the transcription factor known as Elf-1 that is responsible for the transcriptional activation of the zeta chain gene is defective in patients with SLE. Two groups of patients were defined. In the first, Elf-1 was not phosphorylated. In the second, it was phosphorylated in the wrong place.

The number of subjects enrolled to the study since last APR at WRAMC is 31 and the total enrolled to date at WRAMC is 141.

### CONCLUSIONS

Zeta chain expression is defective in patients with SLE and decreased transcription of the zeta chain gene is responsible for this. In the future, replacement of the zeta chain may represent a new modality to treat patients with SLE.

## DETAIL SUMMARY SHEET

TITLE: Cooperative Gynecologic Oncology Group

KEYWORDS: gynecologic, oncology, group

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 31 January 1974  
Umbrella Study

### STUDY OBJECTIVE

Walter Reed section of Gynecologic Oncology is involved with the nationally organized Gynecologic Oncology Group, consisting of forty major medical centers in the country interested in the area of gynecologic tumors and the treatment of gynecologic cancer. The GOG is recognized and funded through the National Cancer Institute.

### TECHNICAL APPROACH

Walter Reed is active in approximately 48 GOG protocols. Presently, there are approximately 60 protocols that are either active or continue to provide significant data. These protocols involve treatment of ovarian carcinoma, cervical carcinoma, adenocarcinoma of the endometrium, uterine sarcoma, vulvar carcinoma, and gestational trophoblastic disease.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Approximately 1195 patients have been entered into GOG protocols from WRAMC with 43 during this year. The total enrolled to date at WRAMC is 1195.

### CONCLUSIONS

Detailed in individual reports.

## DETAIL SUMMARY SHEET

TITLE: GOG 86A - Master Protocol for Phase II Drug Studies in Treatment of Advanced or Recurrent Carcinoma of the Endometrium

KEYWORDS: advanced, carcinoma, endometrium

PRINCIPAL INVESTIGATOR: LTC G. Scott Rose MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 29 April 1986  
Master Protocol

### STUDY OBJECTIVE

To identify additional active agents for treating advanced or recurrent endometrial adenocarcinoma by studying single new drugs in patients with this disease who have not been previously exposed to chemotherapy.

### TECHNICAL APPROACH

Patients must have histologically confirmed advanced, persistent, or recurrent endometrial carcinoma with documented disease progression after local therapy. All patients must have measurable disease. Patients must have failed local therapeutic measures or must be considered incurable with local therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This is a master protocol. Please see individual protocols for further information.

### CONCLUSIONS

See individual protocols for further information.

## DETAIL SUMMARY SHEET

TITLE: GOG 87A - Master Protocol for Phase II Drug Studies in the Treatment of Recurrent or Advanced Uterine Sarcomas

KEYWORDS: advanced, uterus, sarcoma

PRINCIPAL INVESTIGATOR: LTC G. Scott Rose MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 27 May 1986

### STUDY OBJECTIVE

To allow the best possible chance for a new cytotoxic agent to demonstrate activity, this study constitutes a Phase II design in a population of patients who have had no prior drug therapy.

### TECHNICAL APPROACH

To treat an average sample size of thirty patients per drug studied for each of the following cell categories: mixed mesodermal tumor, leiomyosarcoma, and other sarcomas. Patients will have histological confirmed advanced, persistent, or recurrent uterine sarcoma with documented disease progression after appropriate local therapy. Each patient will receive a chemotherapeutic regimen as outlined in each segment of the protocol.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This is a master protocol. Please see individual protocols for further information.

### CONCLUSIONS

See individual protocols for further information.

## DETAIL SUMMARY SHEET

TITLE: GOG 90 - Evaluation of Cisplatin, Etoposide, and Bleomycin (BEP) Induction Followed by Vincristine, Dactinomycin, and Cyclophosphamide (VAC) Consolidation in Advanced Ovarian Germ Cell Tumors, Phase II

KEYWORDS: ovarian, germ cell, tumors

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 31 March 1987

### STUDY OBJECTIVE

To evaluate the effect of induction chemotherapy with cisplatin plus etoposide plus bleomycin (BEP), followed by consolidation with vincristine plus dactinomycin plus cyclophosphamide (VAC) in previously untreated patients with advanced ovarian germ cell tumors.

### TECHNICAL APPROACH

Eligible patients include those with histologically confirmed malignant germ cell tumors of the ovary who have incompletely resected Stage II, III, or IV disease. Patients who have previously received pelvic radiation therapy will be eligible, but the initial dose of etoposide will be reduced 20%.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since the last APR, no new publications involving this study have been produced.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 131, if multi-site study. Grade 4 toxicities include: 45 leukopenia, 15 thrombocytopenia, 76 granulocytopenia, 5 GI, 2 fever, 4 anemia, 1 pulmonary, 1 allergic reaction, 1 hepatic, 1 metabolic, 1 sepsis, 1 leukemia/death. This protocol was closed to patient entry as of 7/27/98.

Ref: Jan 99 and Jul 02 Statistical Reports.

### CONCLUSIONS

1. Data from this and other studies have identified patients that should and should not undergo second look laparotomy.
2. Patients with advanced dysgerminoma have a very high response rate to chemotherapy.

## DETAIL SUMMARY SHEET

TITLE: GOG 95 - Randomized Clinical Trial for the Treatment of Women with Selected Stage IC and II (A, B, C) and Selected Stage IAi and IBi and IAii and IBii Ovarian Cancer, Phase III

KEYWORDS: randomized, ovarian, cancer

PRINCIPAL INVESTIGATOR: LTC G. Scott Rose, MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 26 May 1987

### STUDY OBJECTIVE

This study seeks to compare the progression-free interval and overall survival between p32 and a combination of cyclophosphamide and cisplatin for patients with early ovarian cancer and to determine the patterns of relapse for each form of therapy.

### TECHNICAL APPROACH

All patients must have a histopathologic diagnosis of epithelial ovarian cancer of each histologic cell type: serous mucinous; others include endometrioid, transitional mesonephroid (clear cell), adenocarcinoma (endometrioid with squamous metaplasia), mixed epithelial, and unclassifiable (undifferentiated).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's last review, there have been no additional publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 6. The total number enrolled study-wide is 251, if multi-site study. Grade 4 toxicities include 86 neutropenic episodes, 4 thrombocytopenias, and 1 GI. Two patients experienced small bowel perforation during p32 administration. There have been two treatment related deaths. This protocol was closed to patient accrual on 14 March 1994.

### CONCLUSIONS

After adjusting for stage and histologic grade, the recurrence rate on the cisplatin regimen is 34% lower than the p32 regimen. Estimated relative risk is 0.659 (95% confidence interval: 0.403-1.076).



## DETAIL SUMMARY SHEET

TITLE: GOG 93 - Evaluation of Intraperitoneal Chromic Phosphate Suspension Therapy Following Negative Second-Look Laparotomy for Epithelial Ovarian Carcinoma, Stage III, Phase III

KEYWORDS: chromic phosphate, ovarian, carcinoma

PRINCIPAL INVESTIGATOR: G. Scott Rose, LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 28 July 1987

### STUDY OBJECTIVE

To evaluate the role of intraperitoneal chromic phosphate suspension therapy in patients with Stage III epithelial ovarian carcinoma who have no detectable evidence of disease at the second-look laparotomy.

### TECHNICAL APPROACH

Patients will be given Topotecan  $1.5 \text{ mg/m}^2$  IV over 24 hours every three weeks until progression of disease or adverse effects prohibit further therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since the protocol's review one year ago, there have been no new publications reporting data involving this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 267, if multi-site study.

### CONCLUSIONS

No significant differences were noted in the progression-free and overall survival between the intraperitoneal chromic phosphate treatment group and the observation group.

## DETAIL SUMMARY SHEET

TITLE: GOG 78 - Evaluation of Adjuvant Vinblastine, Bleomycin and Cisplatin Therapy in Totally Reducing Choriocarcinoma, Endodermal Sinus Tumor or Embryonal Carcinoma of the Ovary, Pure and Mixed with Other Elements, Phase II

KEYWORDS: VP-16, bleomycin, cisplatin

PRINCIPAL INVESTIGATOR: Rose G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 29 September 1987

### STUDY OBJECTIVE

To evaluate the effect of adjuvant VP-16, bleomycin, and cisplatin chemotherapy in patients with endodermal sinus tumor, choriocarcinoma, embryonal carcinoma, and grades 2 and 3 immature teratoma of the ovary after removal of all gross tumors.

### TECHNICAL APPROACH

Eligible patients include those with histologically confirmed Stage I choriocarcinoma, endodermal sinus tumor, embryonal carcinoma, and grades 2 and 3 immature teratoma. Patients with Stage II and III disease are also eligible if all gross tumor is removed. Serum AFP and beta-HCG levels should be normal.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 117, if multi-site study. No new toxicities have been reported since the last APR. This study was closed to patient accrual 10 Feb 1992.

### CONCLUSIONS:

This trial confirmed the effectiveness of BEP in patients with ovarian germ cell tumors who have been initially completely resected. Nearly all patients treated this way will survive free of cancer. Short and long-term morbidity is acceptable.

## DETAIL SUMMARY SHEET

TITLE: GOG 99 - A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma

KEYWORDS: radiation, endometrial, adenocarcinoma

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 27 October 2003  
New Anniversary Month: September

### STUDY OBJECTIVE

1) To determine if patients with intermediate-risk endometrial adenocarcinoma who have no spread of disease to their lymph nodes benefit from postoperative pelvic radiotherapy, and 2) evaluate how the addition of pelvic radiotherapy will alter the site and rate of cancer recurrence in these intermediate-risk patients.

### TECHNICAL APPROACH

Patients with primary histologically confirmed grades 2 and 3 endometrial adenocarcinoma are eligible. Patients must have had a total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node sampling, pelvic washings, and found to be surgical Stage I. Patients must have myometrial invasion.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's last review there have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 9 (1 now deceased). The total number enrolled study-wide is 448, if multi-site study.

### CONCLUSIONS

The use of adjuvant RT in women with intermediate risk endometrial cancer decreases the risk of recurrences, but has an inappreciable effect on overall survival.

## DETAIL SUMMARY SHEET

TITLE: GOG 76A - Master Protocol for Phase II Drug Studies in the Treatment of Advanced or Recurrent Squamous Cell Carcinoma of the Cervix

KEYWORDS: advanced, squamous cell carcinoma, cervix

PRINCIPAL INVESTIGATOR: G. Scott Rose, LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 26 July 1988

### STUDY OBJECTIVE

To continue identification of new active drugs in the treatment of advanced or recurrent squamous cell carcinoma of the cervix so that combinations of cytotoxic drugs can be formed which might lead to an improved complete remission rate.

### TECHNICAL APPROACH

Patients enrolled in individual protocols under this Master Protocol will have histologically confirmed, advanced, persistent, or recurrent squamous cell carcinoma of the cervix with documented disease progression after local therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This is a master protocol. Please see individual protocols for further information.

### CONCLUSIONS

See individual protocols.

## DETAIL SUMMARY SHEET

TITLE: GOG 104 - Intraperitoneal Cisplatin/Intravenous Cyclophosphamide Vs. Intravenous Cisplatin/Intravenous Cyclophosphamide in Patients with Nonmeasurable Disease Stage III Ovarian Cancer, Phase III

KEYWORDS: cisplatin, cyclophosphamide, ovary

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 31 January 1989

### STUDY OBJECTIVE

To carry out a Phase III randomized trial of intermediate dose intraperitoneal cisplatin plus intravenous cyclophosphamide versus intermediate dose intravenous cisplatin plus intravenous cyclophosphamide for optimal Stage III ovarian cancer.

### TECHNICAL APPROACH

Patients will be randomized to receive one of the two regimens listed above. Eligible patients must have a histologically confirmed pure epithelial ovarian carcinoma. Those with a borderline tumor will be excluded.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Two abstracts have been presented (1990 and 1995). One manuscript has been published and one is in press. The number of subjects enrolled to the study since last APR is 0. The total enrolled to date at WRAMC is 4. The total number enrolled study-wide is 649. Grade 4 toxicities include 1 abdominal pain, 20 anemia, 5 anorexia, 1 anxiety/depression, 1 clinical hearing loss, 3 creatinine, 1 dehydration, 2 infection, 1 edema, 189 granulocytopenia, 5 hepatic-bilirubin, 1 hypotension, 53 leukopenia, 2 nausea/vomiting, 2 pulmonary, 1 renal creatinine clearance, 1 renal-other, 1 sepsis, 1 stomatitis, 15 thrombocytopenia, and 1 vision. Protocol was closed to patient enrollment effective 15 July 1992.

### CONCLUSIONS

The ovarian cancer patients with optimally debulked (less than 2cm residual tumor mass) Stage III disease, IP administration of cisplatin is associated with statistically significant prolongation of survival and fewer incidences of clinical hearing loss, tinnitus, granulocytopenia, leukopenia, and thrombocytopenia. The IV administration has fewer incidences of abdominal pain and cramping. The IP administration is recommended for cisplatin treatment of this patient population.

## DETAIL SUMMARY SHEET

TITLE: GOG 120 - A Randomized Comparison of Hydroxyurea vs. Hydroxyurea, 5-FU Infusion, and Cisplatin vs. Weekly Cisplatin as Adjunct to Radiation Therapy in Patients with Stages II-B, III, or IV-A Carcinoma of the Cervix and Negative Para-Aortic Nodes

KEYWORDS: cervix, carcinoma, Phase III

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology

STATUS: O  
APPROVAL DATE: 30 June 1992

### STUDY OBJECTIVE

To determine whether hydroxyurea; hydroxyurea, 5-FU infusion plus bolus cisplatin, or weekly cisplatin is superior as a potentiator of radiation therapy in locally advanced cervical carcinoma.

### TECHNICAL APPROACH

Patients with cervical carcinoma (Stages IIB, IIA, IIIB, or IVA) will undergo extraperitoneal staging surgery. Those patients with negative para-aortic nodes will then be randomized to receive radiotherapy plus either: 1) cisplatin; 2) cisplatin, 5FU, and hydroxyurea; or 3) hydroxyurea. Following the completion of therapy, the patients will be followed clinically.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 5. The total number enrolled study-wide is 575, if multi-site study. Grade IV toxicities reported are 36 hematologic, 30 GI, 8 GU, 1 neurologic, 6 cutaneous, 1 fever, 2 hypomagnesemia. Protocol was closed to patient entry 21 April 1997.

### CONCLUSIONS

Cisplatin based chemotherapy and radiation is more effective than chemotherapy and radiation with hydroxyurea. The weekly cisplatin regimen is less toxic than the three-drug cisplatin-containing regimen.

## DETAIL SUMMARY SHEET

TITLE: GOG 136 - Acquisition of Human Ovarian and Other Tissue Specimens and Serum to be Used in Studying the Causes, Diagnosis, Prevention and Treatment of Cancer

KEYWORDS: ovarian, tissue, collection

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 25 August 1992

### STUDY OBJECTIVE

To: 1) accomplish the collection of human ovarian tissue specimens and serum within GOG participating institutions; and 2) provide a long-term storage repository for ovarian tumors and serum. The material will be used in studies to better understand the molecular biology of ovarian tumors.

### TECHNICAL APPROACH

All patients who have had ovarian tumor tissue or extra-ovarian peritoneal serous carcinoma tissue removed are eligible. All patients who have had ovaries removed because of a family history of ovarian cancer are eligible. The tissue, when removed, is shipped along with serum specimens to the GOG repository facility.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

According to GOG Statistical Report there have been at least 103 papers and 30 abstracts that have been generated using tissue bank materials. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 103. The total number enrolled study-wide is 4413, if multi-site study.

Ref: Jan 03 GOG Statistical Report.

### CONCLUSIONS:

None.

## DETAIL SUMMARY SHEET

TITLE: GOG 134 - A Phase III Trial of Taxol at Three Dose Levels and G-CSF at Two Dose Levels in Platinum-Resistant Ovarian Carcinoma

KEYWORDS: taxol, ovarian, G-CSF

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 29 September 1992

### STUDY OBJECTIVE

To: 1) determine if taxol at different dose levels affects response rate, progression-free interval, or survival in patients with platinum-resistant ovarian cancer; 2) compare toxicities of the regimens; and 3) compare the efficacy and toxicity of G-CSF in patients receiving high-dose taxol.

### TECHNICAL APPROACH

Patients with platinum-resistant ovarian epithelial cancer with clinically measurable disease will be randomized to receive taxol at three different dose levels. Patients at the highest dose level will also receive G-CSF at one of two dose levels. Patients are then followed clinically to assess response.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No new publications relating to this study have been published since the last APR. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 6. The total number enrolled study-wide is 449, if multi-site study. No new toxicities have been reported since last APR. This study was closed to patient accrual on 6 February 1995.

### CONCLUSIONS

Prognostic factors associated with survival and PFS include prior platinum resistance, measurable disease, mucinous or clear cell histology and poor performance score.

Doubling the dose of G-CSF did not reduce the frequency of neutropenic fever following the first course of treatment.



## DETAIL SUMMARY SHEET

TITLE: GOG 122 - Whole Abdominal Radiotherapy vs. Combination Doxorubicin-Cisplatin Chemotherapy in Advanced Endometrial Carcinoma

KEYWORDS: radiation, endometrial, chemotherapy

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 27 October 1992

### STUDY OBJECTIVE

1) To assess treatment outcomes (survival and progression-free interval) and failure patterns for advanced Stages III and IV endometrial adenocarcinoma patients using adjuvant, whole, abdominal radiation therapy vs. combination intravenous chemotherapy, and 2) treatment toxicities of either therapy.

### TECHNICAL APPROACH

All patients with endometrial carcinoma undergo surgical staging (TAH, BSO, LNS) and in advanced stage disease are randomized to adjuvant whole abdominal radiation (tele-therapy) vs. combination intravenous doxorubicin-cisplatin chemotherapy every three weeks for eight courses.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's last review, there have been no publications reporting data from this study with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 4. The total number enrolled study-wide is 422, if multi-site study. Grade IV toxicities include 34 WBC, 124 ANC, 21 platelets, 6 other hematological, 130 max hematological, 14 gastrointestinal, 2 hepatic, 2 genitourinary, 6 cardiac, 2 vascular, 1 pulmonary, 2 neurological, 1 fatigue, 6 sepsis/infection, 3 fever, and 1 dermatological. There were no adverse events for WRAMC. This protocol was closed to patient entry effective 25 February 2000.

Ref: Jul 02 GOG Statistical Report

### CONCLUSIONS

Final analysis of recurrence-free survival data is underway.

## DETAIL SUMMARY SHEET

TITLE: GOG 122 - Whole Abdominal Radiotherapy vs. Combination Doxorubicin-Cisplatin Chemotherapy in Advanced Endometrial Carcinoma

KEYWORDS: radiation, endometrial, chemotherapy

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 27 October 1992  
New Anniversary Month: September

### STUDY OBJECTIVE

1) To assess treatment outcomes (survival and progression-free interval) and failure patterns for advanced Stages III and IV endometrial adenocarcinoma patients using adjuvant, whole, abdominal radiation therapy vs. combination intravenous chemotherapy, and 2) treatment toxicities of either therapy.

### TECHNICAL APPROACH

All patients with endometrial carcinoma undergo surgical staging (TAH, BSO, LNS) and in advanced stage disease are randomized to adjuvant whole abdominal radiation (tele-therapy) vs. combination intravenous doxorubicin-cisplatin chemotherapy every 3 weeks for eight courses.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's last review there have been no publications reporting data from this study with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 4 (1 now deceased). The total number enrolled study-wide is 422, if multi-site study. Grade IV toxicities include 34 WBC, 124 ANC, 21 platelets, 6 other hematologic, 130 max hematologic, 14 gastrointestinal, 2 hepatic, 2 genitourinary, 6 cardiac, 2 vascular, 1 pulmonary, 2 neurologic, 1 fatigue, 6 sepsis/infection, 3 fever and 1 dermatologic. There were no reported adverse events for WRAMC. This protocol was closed to patient entry effective 2/25/00.

Ref: July 03 GOG Statistical Report

### CONCLUSIONS

Final analysis of recurrence-free survival data is underway.

## DETAIL SUMMARY SHEET

TITLE: GOG 140 - An Assessment of Age and Other Factors Influencing Protocol vs. Alternative Treatments for Patients with Epithelial Ovarian Cancer Referred to Gynecologic Oncology Group Institutions

KEYWORDS: familial, carcinoma, genetics

PRINCIPAL INVESTIGATOR: Maxwell, G. Larry MAJ MC

ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 30 November 1993

### STUDY OBJECTIVE

To assess the frequency at which patients with ovarian cancer enroll in prospective clinical studies. To assess whether age effects enrollment vs. other demographic or clinicopathological factors.

### TECHNICAL APPROACH (Describe the methodology and note any modifications.)

All patients with primary ovarian carcinoma, including low malignant potential tumors, will fill out a patient questionnaire.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 24. The total number enrolled study-wide is 982, if multi-site study. There were no reportable adverse events. This protocol was closed to patient entry 2/5/96.

Ref: Jul 02 GOG Statistical Report

### CONCLUSIONS

Among patients entered on this protocol there is a significant relationship between age at diagnosis and stage of disease at diagnosis. In fact older patients tend to present with more advanced disease than younger patients.

This preliminary analysis suggests that among early stage patients, few are enrolled on GOG studies and this does not vary by age. However, among advanced stage patients entered on this survey study, 36% of younger patients compared to 26% of older patients were enrolled on GOG clinical studies. Further analysis is underway to investigate whether the relationship of age to planned treatment among advanced stage patients can be explained by other coexisting medical conditions related to the aging process.

The validity of this study depends upon the extent to which patients were "captured" for this study at each participating institution. Information is being collected from tumor registries to assess the number of patients missed and the reasons for failing to capture these patients.

## DETAIL SUMMARY SHEET

TITLE: GOG 26LL - A Phase II Trial of Prolonged Oral Etoposide (VP-16) in Patients with Advanced Pelvic Malignancies

KEYWORDS: carcinoma, chemotherapy, pelvic

PRINCIPAL INVESTIGATOR: LTC G. Scott Rose, MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 21 December 1993

### STUDY OBJECTIVE

To determine the efficacy of oral etoposide in patients with advanced pelvic malignancies.

### TECHNICAL APPROACH

Patients with histologically confirmed recurrent or metastatic gynecologic cancer refractory to standard therapy with measurable disease receive oral VP-16 on days 1-21 monthly. Treatment continues until response or toxicity occurs.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 6. The total number enrolled study-wide is 151, if multi-site study. Grade 4 toxicities include 10 leukopenia, 4 thrombocytopenia, 14 neutropenia, 1 GI, 4 anemias, 1 pulmonary, and 1 infection. No toxicities reported for WRAMC. Study met accrual goal and closed to patient entry 09/05/00.

Ref: July 02 GOG Statistical Report

### CONCLUSIONS

There is evidence of activity with this regimen in patients with recurrent epithelial ovarian carcinoma. Phase I studies of dose escalating oral Etoposide in combination are being conducted in untreated and previously treated ovarian carcinoma.

## DETAIL SUMMARY SHEET

TITLE: GOG 109 - A Randomized Comparison of 5-FU Infusion and Bolus Cisplatin as an Adjunct to Radiation Therapy Alone in Selected Patients with Stages I-A2, I-B, and II-A Carcinoma of the Cervix Following Radical Hysterectomy and Node Dissection Phase III Inter

KEYWORDS: cisplatin, radiation, cervix

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 21 December 1993

### STUDY OBJECTIVE

To determine whether the combination of 5-fluorouracil (5FU) and cisplatin used as an adjunct to radiation therapy will improve survival rate or progression-free survival and decrease extra pelvic failure compared to radiation therapy alone in patients with positive parametrial involvement or positive surgical margins following radical hysterectomy and lymph node dissection for Stages I-A2, IB, and IIA carcinoma of the cervix.

### TECHNICAL APPROACH

Patients with Stage IA2, IB, and IIA invasive squamous, adeno or adenosquamous carcinoma of the cervix, status post radical hysterectomy with histologically positive lymph nodes, parametria, or surgical margins will be enrolled. Patients will receive standard whole pelvic radiation with or without chemosensitization.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since the last review, there have been no new publications reported.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 226, if multi-site study. Grade 4 toxicities include 1 anemia, 1 cardiac, 5 diarrhea, 2 dyspnea, 12 granulocytopenia, 1 infection, 3 leukopenia, 1 skin ulceration (non-local), 2 small bowel obstruction, 1 stomatitis, and 3 vomiting. No toxicities were reported for WRAMC. The protocol was closed to patient entry effective 12/15/96.

Ref: July 02 GOG Statistical Report

### CONCLUSIONS

It concluded that the addition of chemotherapy to radiation therapy significantly improves progression-free and overall survival for high-risk, Stage I-A2 through II-A patients who undergo radical hysterectomy and pelvic lymphadenectomy for carcinoma of the cervix.

## DETAIL SUMMARY SHEET

TITLE: GOG 123 - A Randomized Comparison of Radiation Therapy and Adjuvant Hysterectomy vs. Radiation Therapy and Weekly Cisplatin and Adjuvant Hysterectomy in Patients with Bulky Stage IB Carcinoma of the Cervix (Phase III)

KEYWORDS: carcinoma, cervix, radiation

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 21 December 1993

### STUDY OBJECTIVE

To determine if weekly cisplatin infusion improves local-regional control and survival when added to radiation therapy and extrafascial hysterectomy. Also, to determine the toxicities of these two treatments.

### TECHNICAL APPROACH

Patients with bulky IB and barrel-shaped cervical invasive squamous, adeno, or adenosquamous carcinomas who have surgically-negative pelvic/para-aortic nodes receive either whole pelvic radiation with or without cisplatin chemosensitization followed by extrafascial hysterectomy

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no new publications reported since the last APR.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 374, if multi-site study. Grade 4 toxicities include 6 hematologic, 14 GI, 3 GU, 1 cardiovascular, and 1 cutaneous. This study was closed April 7, 1997 to patient accrual.

Ref: July 02 GOG Statistical Report

### CONCLUSIONS

The addition of weekly cisplatin during irradiation was associated with a reduction in risk of recurrence of 49% and a risk of death 46%. Both statistics were highly significant.

## DETAIL SUMMARY SHEET

TITLE: GOG #150 - A Phase III Randomized Study of Whole Abdominal Radiotherapy (WAR) versus Combination Ifosfamide-Mesna with Cisplatin in Optimally Debulked Stage I, II, III or IV Carcinosarcoma (CS) of the Uterus

KEYWORDS: uterine, sarcoma, therapy

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 25 January 1994

### STUDY OBJECTIVE

To compare outcomes and failure patterns in patients with Stage I-IV uterine carcinosarcoma treated with whole abdominal radiotherapy vs. combination chemotherapy with cisplatin/ifosfamide/mesna. Also, to compare toxicities of two regimens.

### TECHNICAL APPROACH

All eligible patients will be enrolled who have had surgical Stage I-IV disease, s/o TAH, BSO, and maximal resection of macroscopic abdomino-pelvic lesions (including lymph nodes) to greater than 1 cm disease. All patients less than 8 weeks post-op will be randomized to either program.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been no publications reporting data from studies with similar study design in the literature. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 178, if multi-site study. 161 of these were evaluable. Grade 4 toxicities include 1 anemia, 4 GI, 1 hepatic, 1 infection, 3 cardiovascular, 1 pulmonary. Grade 4 late effects (adverse events which occurred or persisted after completing study treatment) include 1 GI, 2 hepatic, and 0 other. (Reference: GOG Statistical Report, July 2002.)

### CONCLUSIONS

Too early. Study still in the accrual stage.

## DETAIL SUMMARY SHEET

**TITLE:** GOG 152 - A Phase II Randomized Study of Cisplatin (NSC #119875) and Taxol (Paclitaxel) (NSC #125973) with Interval Secondary Cytoreduction Versus Cisplatin and Paclitaxel in Patients with Suboptimal Stage III Epithelial Ovarian Carcinoma

**KEYWORDS:** ovary, cancer, chemotherapy

**PRINCIPAL INVESTIGATOR:** LTC G. Scott Rose, MC

**DEPARTMENT:** Obstetrics & Gynecology

**STATUS:** O

**SERVICE:** Gynecologic Oncology Group

**INITIAL APPROVAL DATE:** 31 May 1994

### STUDY OBJECTIVE

To determine if secondary cytoreduction contributes to progression-free interval and survival in patients with suboptimally debulked Stage III and IV epithelial ovarian cancer. Also, to determine the morbidity of the cytoreduction surgery.

### TECHNICAL APPROACH

Suboptimal debulked Stage III and IV ovarian epithelial cancer patients receive three courses of taxol/cisplatin intravenously. Patients who respond are randomized to an interim cytoreduction followed by three additional courses of taxol/cisplatin versus no surgery but three courses of taxol/cisplatin.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's last review, there has been no publication reporting data for this study. This study was closed to patient entry effective 29 January 2001. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 7. The total number enrolled study-wide is 550, if multi-site study. The following table summarizes Grade 4 Toxicities after randomization.

Adverse Effect	Debulking (n=216)	No Debulking (n=209)
	Grade 4 Toxicity (%) *	Grade 4 Toxicity (%) *
Leukopenia**	6.3	4.8
Granulocytopenia**	72.0	74.0
Thrombocytopenia * *	0.0	0.5
GI	6.5	4.3
Pulmonary	0.9	0.0
Cardiac	1.4	0.9
Neurologic	0.0	0.5
Infection	0.5	0.0
Metabolic	0.9	0.0

\*Percent of patients randomized to the treatment groups.

\*\*10 patients were not evaluated.

### CONCLUSIONS

Interval secondary cytoreductive surgery does not improve progression-free or overall survival in patients who have previously undergone maximal primary cytoreduction.



## DETAIL SUMMARY SHEET

TITLE: GOG 157 - A Randomized Phase II Trial of Carboplatin (AUC 7.5) and Paclitaxel 175 mg/m<sup>2</sup> q 21 Days X Three Courses vs. the Same Regimen X Six Courses, in Patients with Selected Stage IC and II (A, B, C) and Selected IA and IB Ovarian Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 28 March 1995

STUDY OBJECTIVE

To evaluate any chemotherapy schedule dependence in the treatment of early-stage ovarian cancer.

TECHNICAL APPROACH

This is a Phase III protocol studying the difference between three vs. six cycles of taxol carboplatin in patients having early-stage ovarian cancer.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications since the last APR. We are awaiting the first draft.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 8. The total number enrolled study-wide is 457, if multi-site study. Grade 4 toxicities include 9 leukopenia, 191 granulocytopenia, 41 thrombocytopenia, 1 anemia, 9 GI, 2 neurologic, 1 infection and 4 allergy. This study was closed to patient accrual effective 5/25/98.

CONCLUSIONS

There is insufficient evidence to reject the null hypothesis that the recurrence rates are unaltered by adding three additional courses over and above the standard three courses of carboplatin and paclitaxel.

## DETAIL SUMMARY SHEET

TITLE: GOG 158 - A Phase III Randomized Study of Cisplatin and Paclitaxel (24-Hour Infusion) vs. Carboplatin and Paclitaxel (3-Hour Infusion) in Optimal Stage III Epithelial Ovarian Carcinoma

KEYWORDS: cisplatin, paclitaxel, ovarian

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 25 August 1992

### STUDY OBJECTIVE

To compare recurrence-free interval and survival in patients with less than or equal to 1 cm residual Stage III epithelial ovarian cancer receiving cisplatin and paclitaxel administered by a 24-hour infusion vs. carboplatin plus paclitaxel administered by a three-hour infusion.

### TECHNICAL APPROACH

This is a Phase III study. Patients must have histologic diagnosis of epithelial ovarian cancer Stage III with less than or equal to 1 cm residual disease. All patients must have appropriate surgery for ovarian carcinoma.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there has been one additional abstract awaiting first draft of secondary manuscript. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 3 (1 now deceased). The total number enrolled study-wide is 850, if multi-site study. Grade 4 toxicities include 72 leukopenia, 89 thrombocytopenia, 596 other hematologic, 54 GI, 1GU, 2 pulmonary, 6 cardiovascular, 2 neurologic, 3 fever, 9 allergic, 3 fatigue, 8 infection, 10 metabolic, 2 pain, 1 hepatic and 1 lymphatic.

Ref: Jan 03 GOG Statistical Report

### CONCLUSIONS:

The preferred chemotherapy regimen for patients with advanced-stage ovarian cancer consists of paclitaxel plus carboplatin based on less toxicity, ease of administration, and the relative risk confidence intervals for both survival and progression free survival includes, almost exclusively, reductions in risk compared to cisplatin plus paclitaxel.

## DETAIL SUMMARY SHEET

TITLE: GOG 162 - A Phase III Randomized Trial of Cisplatin (NSC #119875) with Paclitaxel (NSC #125973) Administered by Either 24-Hour Infusion or 96-Hour Infusion in Patients with Selected Stage III and Stage IV Epithelial Ovarian Cancer

KEYWORDS: ovary, neoplasm, taxol

PRINCIPAL INVESTIGATOR: LTC G. Scott Rose, MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 28 May 1996

### STUDY OBJECTIVE

To compare progression-free survival, overall survival and frequency of response of 24-hour vs. 96-hour paclitaxel (Taxol) infusions, each combined with cisplatin, in the treatments of selected stage III and stage IV epithelial ovarian cancer. To determine the incidence and severity of adverse events, including catheter complications and chemotherapy toxicity, for 96-hour infusions of paclitaxel. To examine the relationship between plasma paclitaxel concentrations and measures of drug toxicity and response in both 24-hour and 96- hour infusion schedules.

### TECHNICAL APPROACH

This is a Phase III trial randomizing between 24-hour and 96-hour taxol infusions in patients with advanced ovarian carcinoma.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data from this study or from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 7. The total number enrolled study-wide is 293, if multi-site study. Grade 4 toxicities 50 leukopenia, 189 granulocytopenia, 11 thrombocytopenia, 1 anemia, 31 GI, 1 GU, 2 renal, 1 hepatic, 4 pulmonary, 5 cardiac, 10 infection, 1 pain, 2 central neuropathy, 2 allergy, and 8 metabolic. WRAMC had 1 patient reporting with adverse reaction. This study was closed to patient accrual effective 2 August 2000.

### CONCLUSIONS

Prolonged infusion of paclitaxel for 96 hours followed by cisplatin does not significantly increase progression-free survival or overall survival when compared to 24-hour infusion of paclitaxel followed by cisplatin. However, granulocytopenia occurs with greater severity on the 24-hour infusion regimen.

## DETAIL SUMMARY SHEET

**TITLE:** GOG # LAP2 - A Phase III Randomized Clinical Trial of Laparoscopic Pelvic and Para-Aortic Node Sampling with Vaginal Hysterectomy and BSO vs. Open Laparotomy with Pelvic and Para-Aortic Node Sampling and Abdominal Hysterectomy and BSO in Endometrial Adenocarcinoma, Clinical Stages I, IIA, Grades I, II, and III

**KEYWORDS:** laparoscopy, lymphadenectomy, endometrium

**PRINCIPAL INVESTIGATOR:** G. Scott Rose, LTC MC

**DEPARTMENT:** Obstetrics & Gynecology

**STATUS:** O

**SERVICE:** Gynecologic Oncology Group

**INITIAL APPROVAL DATE:** 30 July 1996

### STUDY OBJECTIVE

- a. To compare the incidence of surgical complications, peri-operative morbidity and mortality which occurs with surgical staging via either laparoscopic assisted vaginal hysterectomy or a total abdominal hysterectomy in patients with clinical stage I or IIA endometrial cancer.
- b. To compare the length of hospital stay following surgery for these patients staged with these two surgical techniques.
- c. To compare post-operative self assessed quality of life scores in patients staged with these two surgical techniques.

### TECHNICAL APPROACH

Patients will be randomized to either laparoscopic assisted vaginal hysterectomy or a total abdominal hysterectomy. Patients will be followed post op for complications/quality of life.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since last year's submission, no new publications reporting data from studies with similar design.

Post surgical adverse effects are presented for 1,297 patients with follow-up data submitted and data are pending for 18 cases.

Adverse Effect	Grade					Total
	0	1	2	3	4	
Urinary tract infection	1223	41	26	4	3	1297
Fever	1157	89	45	4	2	1297
Pelvic cellulitis	1277	12	6	1	1	1297
Pelvic or extremity thrombosis	1288	0	2	7	0	1297
Abscess	1288	1	0	5	3	1297
Pulmonary embolus	1281	0	1	1	14	1297
Bowel obstruction	1284	2	2	4	5	1297
Ileus	1189	51	27	26	4	1297
Pneumonia	1277	6	6	6	2	1297
Abdominal wound infection	1240	28	18	11	0	1297
Urinary fistula	1293	0	0	2	2	1297
Bowel fistula	1292	2	0	1	2	1297

The number of subjects enrolled to the study since last APR at WRAMC is 15 and the total enrolled to date at WRAMC is 43. The total number enrolled study-wide is 1657, if multi-site study.

**CONCLUSIONS:** None. Too early.

## DETAIL SUMMARY SHEET

TITLE: GOG #9302 – Laparoscopic Staging in Patients with Incompletely Staged Cancer of the Ovary, Primary Fallopian Tube Carcinoma and Primary Peritoneal Carcinoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC

ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology

STATUS: O

SERVICE: Gynecologic Oncology Group

INITIAL APPROVAL DATE: 17 December 1996

### STUDY OBJECTIVE

To determine the feasibility of performing laparoscopic staging in those patients incompletely staged by laparotomy. To evaluate the adverse effects related to laparoscopic staging.

### TECHNICAL APPROACH

Laparoscopy will replace a second laparotomy in those patients incompletely staged with ovarian, fallopian tube, or peritoneal cancers.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's last review there is a manuscript preparation.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 7. The total number enrolled study-wide is 73, if multi-site study. No grade 4 toxicities reported. Study met accrual goal and closed to patient entry effective August 28, 2002.

Ref: July 02 GOG Statistical Report.

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: GOG #164 Randomized, Controlled Trial of Salvage TX w/Paclitaxel & Carboplatin vs. Salvage TX w/Stem Cell Supported High-Dose Carboplatin, Mitoxantrone & Cyclophosphamide in Patients w/Persistent Low Volume Ovarian CA

KEYWORDS: ovarian, chemotherapy, bone marrow

PRINCIPAL INVESTIGATOR: LTC G. Scott Rose MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: C  
INITIAL APPROVAL DATE: 24 April 1997

### STUDY OBJECTIVE

1) To compare outcomes of salvage therapy with either standard dose chemo or bone marrow reconstitution following high dose chemo in patients with drug sensitive, low volume persistent ovarian cancer after standard therapy; 2) to compare the toxicities of these two salvage regimens; 3) to compare selected health related dimensions of quality of life in these two patient populations.

### TECHNICAL APPROACH

This is a phase III trial design of the above. Parameters to be measured include overall survival, progressive free survival, toxicities, and selected quality of life issues.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 24, if multi-site study. This study was closed to patient entry 10 May 1999. This protocol was terminated effective 7 February 2000 due to insufficient accrual rate. No Grade 4 toxicities have been reported to date.

Ref: Jan 02 GOG Statistical Report

### CONCLUSIONS

Study closed and terminated due to insufficient accrual rate.

## DETAIL SUMMARY SHEET

TITLE: GOG 137 - A Randomized Double-Blinded Trial of Estrogen Replacement Therapy Versus Placebo in Women with Stage I or II Endometrial Adenocarcinoma.

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 30 September 1997

### STUDY OBJECTIVE

To determine the effect of estrogen replacement therapy on recurrence free and overall survival in women with a history of stage I and II endometrial adenocarcinoma.

### TECHNICAL APPROACH

Patients are randomized to either receive ERT for three years, or a placebo for three years. Both groups are followed for five years.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study was closed to patient entry effective 30 January 2003. Recent studies have not shown that women with stage I-II endometrial cancers who take estrogen are at any increased risk over women who were not given estrogen to treat their symptoms (American Journal of Obstetrics and Gynecology, 1996, vol. 175, pp. 1195-2000).

In January, the GOG Data Monitoring Committee conducted a review of GOG protocol 0137 and decided that the study will not be able to answer the question about the risk of recurrence and should be stopped. The statisticians involved with the study noted two problems with the study. First, most of the patients being enrolled in the study have very early-stage cancers, with less likelihood of having a cancer recurrence. Second, enrollment in the trial has slowed, possibly because of news reports about hormone replacement therapy (HRT). As a result, there will not be enough evidence to determine whether estrogen replacement therapy (ERT) affects the recurrence of cancer among women with stage I or II endometrial cancer. The study is NOT being stopped because of any evidence of increased risk among the women on the study who received estrogen replacement therapy.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 11. The total number enrolled study-wide is 1240, if multi-site study.

### CONCLUSIONS

Too early to determine.

## DETAIL SUMMARY SHEET

TITLE: GOG 165 - A Randomized Comparison of Radiation Plus Weekly Cisplatin vs. Radiation Plus PVI (Protracted Venous Infusion) 5FU in Patients with Stage IIB, IIIB, and IVA Carcinoma of the Cervix

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 05 February 1998

STUDY OBJECTIVE:

To compare the progression-free survival of patients with advanced cervical cancer limited to the pelvis receiving radiation only to radiation plus weekly cisplatin. To compare the progression free survival of patients with advanced cervical cancer limited to the pelvis receiving radiation plus prolonged venous infusion (PVI) 5-fluorouracil to radiation plus weekly cisplatin. To determine the relative toxicities of radiation plus chemotherapy (either weekly cisplatin or PVI 5 fluorouracil) compared to radiation alone. To compare the progression-free survival and survival of patients with advanced cervical cancer limited to the pelvis whom; (a) smoke at the time of diagnosis and (b) smoke during radiation therapy vs. those who quit.

TECHNICAL APPROACH

This study deals with patients with stage II-B, III-B and IV-A carcinoma of the cervix.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 352, if multi-site study. Grade 4 toxicities include 12 hematologic, 32 GI, 7 GU, 2 pulmonary, 3 metabolic, 2 fatigue, 1 pain, 3 cutaneous, 1 allergy, 2 cardiovascular, 1 hernia, 1 ureter obstruction. This protocol was closed to patient entry effective August 2, 2000.

Ref: Jul 02 GOG Statistical Report

CONCLUSIONS

This study was closed as a result of the GOG Data Monitoring Committee reviewing the results of a planned interim analysis. The interim analysis indicated that the PVI 5-FU treatment group would never, in all likelihood, have a statistically significant better progression free survival compared to weekly cisplatin treatment groups. Under the rules of interim analysis, specifically the futility analysis, the study was closed and the null hypothesis will be accepted (i.e., chemoradiation with PVI 5-FU is not any more efficacious than chemoradiation with weekly cisplatin).



## DETAIL SUMMARY SHEET

TITLE: GOG 161 - A Phase III Trial of Ifosfamide (NSC #109724) vs. Ifosfamide plus Paclitaxel (NSC #125973) in Patients with Advanced, Persistent or Recurrent Carcinosarcoma (Mixed Mesodermal Tumors) of the Uterus

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 24 February 1998

### STUDY OBJECTIVE

To determine whether the addition of paclitaxel improves length of survival, progression-free interval and response rate when compared to ifosfamide alone in previously untreated patients with advanced, persistent or recurrent carcinosarcoma (mixed mesodermal tumors) of the uterus.

### TECHNICAL APPROACH

This is a Phase III trial for patients with advanced, persistent or recurrent carcinosarcomas (mixed mesodermal tumors) of the uterus.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No publications have been reported.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 147, if multi-site study.

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: The Effect of Environmental CO<sub>2</sub> on Thermotolerance-Associated Heat Shock Protein Synthesis

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC

ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology

STATUS: O

SERVICE: Gynecology-Oncology

INITIAL APPROVAL DATE: 02 March 1999

### STUDY OBJECTIVE

To determine if heat shock protein synthesis associated with the development of thermotolerance can be influenced by increasing environmental CO<sub>2</sub> concentration in-vitro.

### TECHNICAL APPROACH

This is a basic service project involving no human subjects. All experiments are derived from established cell line.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are no publications reporting data on this study. This is a Walter Reed study that does not involve human subjects. Work is being done on this study, but there are no results to report.

The number of subjects enrolled to the study since last APR at WRAMC is N/A and the total enrolled to date at WRAMC is N/A.

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: GOG #9902 - Quality of Life of Gynecologic Cancer Survivors (NCI 1 RO1 CA 79039-01)

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC

ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology

STATUS: O

SERVICE: Gynecologic Oncology Group

INITIAL APPROVAL DATE: 21 September 1999

### STUDY OBJECTIVE

To describe the significant quality of life (QOL) concerns and long-term survivorship issues of women who were diagnosed and treated for early-stage ovarian and endometrial cancer five or more years ago.

To identify mechanisms which contribute to a gynecologic cancer survivorship model through comparison and prediction of high versus low QOL associated with long-term adjustment and survivorship.

### TECHNICAL APPROACH

This is a QOL phone interview for survivors who completed GOG clinical trial #95 (ovarian), or GOG clinical trial #99 (endometrial) at least five years and are without recurrent disease.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

One publication on this study was accomplished. See publications listing for specifics. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 6. The total number enrolled study-wide is 162, if multi-site study. This study was closed to patient accrual on 20 January 2002. There were no toxicities reported.

### CONCLUSIONS

None. Too early.

## DETAIL SUMMARY SHEET

TITLE: GOG 167 - A Two-Part Study of the Treatment of Atypical Endometrial Hyperplasia  
Part A: A Prospective Study of Immediate Hysterectomy  
Part B: A Randomized Phase II Study of Medroxyprogesterone Acetate Versus Depo-Provera

### KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 21 September 1999

### STUDY OBJECTIVE

Part A: To estimate and compare the frequency of adenocarcinoma in patients diagnosed with atypical hyperplasia (AEH) at initial biopsy in groups defined by the Study Co-Chairs and those not considered AEH by central review. Given favorable results, Part B will be opened to patient accrual.

Part B: To conduct a randomized phase II trial to determine the frequency of complete remission of atypical endometrial hyperplasia (AEH) in patients treated for three months with oral medroxyprogesterone acetate or Depo-Provera IM.

### TECHNICAL APPROACH

Part A: Patients diagnosed with atypical endometrial hyperplasia and entry onto the study, patients will receive immediate hysterectomy.

Part B: Patients with confirmed diagnosed of endometrial hyperplasia will be randomized to:

Regimen 1: Medroxyprogesterone acetate (MPA) 10mg/po/day continuously for three months.

Regimen 2: Depo-Provera 150mg IM (gluteal or deltoid muscle) Q months for three months.

After three months patients will undergo total hysterectomy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Part A was closed to patient accrual on 24 Feb 03. Part B is not yet accruing patients. One abstract was published regarding this study as is listed at the end of the report. The number of subjects enrolled to the study since last APR at WRAMC is 3 and the total enrolled to date at WRAMC is 14. The total number enrolled study-wide is 306, if multi-site study. Grade 4 adverse effects: 3 hemoglobin, 2 other hematologic, 3 cardiovascular, 1 coagulation, 1 metabolic, 3 pulmonary.

### CONCLUSIONS

None. Too early.

## DETAIL SUMMARY SHEET

TITLE: Intravenous Administration of 1311-6-B Iodomethylnorcholesterol (NP-59) for Adrenal Evaluation and Imaging

KEYWORDS:

PRINCIPAL INVESTIGATOR: Jaime L. Montilla MAJ MC

ASSOCIATES: None

DEPARTMENT: Radiology

SERVICE: Nuclear Medicine

STATUS: O

INITIAL APPROVAL DATE: 24 April 1997

### STUDY OBJECTIVE

Clinical evaluation of NP-59 as a diagnostic agent for the detection of adrenal-cortical disorders.

### TECHNICAL APPROACH

This study will be performed in humans of either sex. NP-59 will be administered by slow intravenous injection with a dose of 2mCi in adults, 15 uCi/kg in children. Lugol's solution, 5 drops twice daily starting one day before injection and continuing for two weeks, will be used to block thyroid uptake of radionuclide. Planar and SPECT images will be obtained on the 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> days after injection using the scintillation camera and the on-line microcomputer. The drug to be used in this study, NP-59 is investigational and will be used under IND number 12605, which is held by the University of Michigan.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 5. No adverse reactions. No Publications.

### CONCLUSIONS

The protocol is ongoing as scheduled.

## DETAIL SUMMARY SHEET

**TITLE:** RTOG 94-08 - A Phase III Trial of the Study of Endocrine Therapy Used as a Cytoreductive and Cytostatic Agent Prior to Radiation Therapy in Good Prognosis Locally-Confin ed Adenocarcinoma of the Prostate

**KEYWORDS:** Zoladex, Flutamide

**PRINCIPAL INVESTIGATOR:** Scott Roberts, MD, Michael Dullea, MAJ MC

**ASSOCIATES:**

**DEPARTMENT:** Radiology  
**SERVICE:** Radiation Therapy

**STATUS:** O  
**INITIAL APPROVAL DATE:** 23 May 1995

### STUDY OBJECTIVE

To evaluate the potential impact of a combination of Zoladex and Flutamide used as cytoreductive agents prior to undergoing definitive radiation therapy in locally confined carcinomas of the prostate.

### TECHNICAL APPROACH

There are two arms to this randomized study for patients with clinical stages T1b-T2b adenocarcinoma of the prostate. The control arm (Arm 2) is radiation therapy only to the prostate and regional lymphatics. The experimental arm (Arm 1) involves the use of total androgen suppression (Zoladex and Flutamide) for 2 months prior and 2 months during radiation therapy to the prostate and regional lymphatics.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The multi-institutional trial opened on October 31, 1994. The targeted accrual was 1980 cases. By October 2001, 1922 cases were entered. At WRAMC, 18 patients were enrolled. Since 1999, no further patients were enrolled through WRAMC. Fourteen patients continue in follow-up. Three patients developed an elevation in liver function tests and Flutamide was discontinued. One patient developed Grade 3 pancytopenia requiring red blood cell transfusions and discontinuation of Flutamide. One patient developed Grade 2 radiation prostatitis and was treated with steroid enemas with improvement. Two deaths have occurred for causes unrelated to prostate cancer. One patient has terminated participation in the study. One patient has been lost to follow-up.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 18. The total number enrolled study-wide is 1922, if multi-site study.

### CONCLUSIONS

This study will provide data on the role of hormonal therapy when combined with external beam RT in the treatment of prostate cancer.

## DETAIL SUMMARY SHEET

**TITLE:** RTOG 94-13 - A Phase III Trial Comparing Whole Pelvic Irradiation Followed by a Conedown Boost to Boost Irradiation Only and Comparing Neoadjuvant Total Androgen Suppression

**KEYWORDS:** radiotherapy, prostate cancer

**PRINCIPAL INVESTIGATOR:** Dr. Scott Roberts

**ASSOCIATES:** Dullea, Michael D. MAJ MC

**DEPARTMENT:** Radiology

**SERVICE:** Radiation Therapy

**STATUS:** O

**INITIAL APPROVAL DATE:** 27 February 1996

### STUDY OBJECTIVE

To determine optimal method of delivery of hormonal therapy with radiotherapy in the treatment of localized prostate cancer. A secondary objective is determination of optimal field size in the delivery of radiotherapy.

### TECHNICAL APPROACH

There are four arms to the study: Arm 1 delivers neoadjuvant and concurrent hormonal therapy with pelvis radiation. Arm 2 delivers neoadjuvant and concurrent hormonal therapy with prostate-only radiation. Arm 3 delivers concurrent and adjuvant hormonal therapy with pelvis radiation. Arm 4 delivers concurrent and adjuvant hormonal therapy with prostate-only radiation.

### PRIOR AND CURRENT PROGRESS

The study was opening nationally on 1 April 1995 and closed on 1 June 1999 with a total enrollment of 1323 cases. The median age for all patients was 70 years and nearly 25% were of African-American origin. The results of the study were presented at a plenary session at the annual meeting of ASTRO in Oct 2001. Patients treated with the whole pelvis radiotherapy (WPRT) experienced a 4 year Progression Free Survival (PFS) of 56% compared to 46% when treated with prostate only radiotherapy (PO RT)  $p=0.014$ , but no difference is yet seen in OS (85 vs 83%,  $p=0.53$ ). Patients treated with neoadjuvant hormonal therapy (NHT) experienced a four-year progression free survival of 53 vs. 48% for adjuvant hormonal therapy versus concurrent hormonal therapy, and the survival advantage is not yet statistically significant (87 vs. 82%,  $p=0.098$ ). When comparing all four arms, there was a PFS advantage for WPRT + NHT (neoadjuvant hormonal therapy) compared to the other arms (61% versus 45, 49, and 47%, respectively,  $p=0.005$ ). However, no OS advantage is yet seen (88 versus 83, 81, and 82%). Grade 3 or higher GU and GI toxicities were not clinically significantly different between treated patients on any of the four arms (3% versus 1%).

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 16. The total number enrolled study-wide is 1,323 patients.

### CONCLUSIONS

The preliminary analysis demonstrated that WPRT with NHT is associated with an improvement in PFS compared to the PORT arms and the concurrent HT arms.

## DETAIL SUMMARY SHEET

**TITLE:** Comparison of Electron Beam Computed Virtual Colonoscopy (EBCT-VC) with Visual Colonoscopy, Using Each Patient as Their Own Control

**KEYWORDS:** Colonoscopy; X-ray computed tomography; Electron beam computed tomography; Colon, Cancer, colon; Polyp; Imaging; Three-dimensional imaging

**PRINCIPAL INVESTIGATOR:** Irwin M. Feuerstein, MD

**ASSOCIATES:** COL Michael P. Brazaitis, MC; CPT Roger Polish, MC; CPT Eric Osgard, MC; COL Roy Wong, MC; Corinne Maydonovitch, BS; Audrey Chang, PhD; Gregory N. Bender, MD

**DEPARTMENT:** Radiology

**STATUS:** C

**SERVICE:** Diagnostic Radiology

**INITIAL APPROVAL DATE:** 23 March 1999

### STUDY OBJECTIVE

To determine whether computed tomography (CT) colography, using electron beam computed tomographic virtual colonoscopy (EBCT-VC) methodology, can identify the normal colon with a high degree of predictability. Secondary information of benefit will be to identify the length of CT colography (CTC) examination time relative to the examination time of colonoscopy, to identify the success rate of CTC in visualizing the entire colon relative to the success rate of colonoscopy to do the same, to identify which examination is more preferable to the patient, and to identify if CTC can be relied upon to such a degree that repeat colonoscopy might be necessary if initially negative in the face of a positive CTC examination.

### TECHNICAL APPROACH

There have been no changes to the technique since the prior APR, and the new technique appears to working quite acceptably. There have been no patient issues, and no scanner failures. Patients will receive virtual and fiberoptic colonoscopy on the same day, with the information conveyed via the patient guardian. Fiberoptic colonoscopy will be done in the standard manner, while virtual colonoscopy will be done on the electron beam scanner with Colyte preparation and air insufflation using a standard tip. Images will be reviewed in both 2- and 3-dimensions with fly-through. The current scans are done without glucagons, and without oral contrast, using air contrast only. The 2-D images continue to be viewed on the Scribe workstation before the fiberoptic study, and fly-through images still viewed on the AccuImage workstation after the fiberoptic study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT

The number of subjects enrolled to the study since last APR at WRAMC is 0. The total enrolled to date is 7.

### CONCLUSIONS

This study was closed in deference to a large, better-funded study. The second study is similar in spirit and design. This protocol was the framework upon which the second study was conceived and designed. There was not enough data collected in this study to support any analyses or conclusions. Because of differences in the techniques used, the data from the patients will not be included in the subsequent study.



## DETAIL SUMMARY SHEET

TITLE: POG 8650 - National Wilm's Tumor Study - A POG Phase III Study

KEYWORDS: Wilms' tumor, renal tumor, nephroblastoma

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, A. COL MC; Crouch, G. LtCol MC; Hartman, K. LTC MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology Oncology

INITIAL APPROVAL DATE: 28 October 1986

### STUDY OBJECTIVE

To 1) gather data on morphology and correlate it with treatment and clinical outcome; and 2) refine clinical trials to reduce therapy to simpler and shorter regimens.

### TECHNICAL APPROACH

To attempt to give the usual five-day course in one day, (has been done with other tumors), and to examine in randomized trial with current therapies.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study closed to accrual effective 1 September 1994. Final accrual as of last reporting to POG (31 Jan 96) is 3335. There were a total of 14 patients registered at WRAMC; the last WRAMC registration was in July 1993. There were no unexpected toxicities reported. Of the 14 WRAMC registrants, 9 are followed at WRAMC and are in remission, 4 transferred to other POG institutions, and 1 died of relapse and progressive disease. Results showed no statistically significant difference in relapse-free survival or survival for patients treated with short versus long treatment regimens. No new outcome analyses have been reported since the last COG Study Report from the Spring 2001 COG Meeting.

### CONCLUSIONS

Study should remain open for data collection for patients followed at WRAMC.

## DETAIL SUMMARY SHEET

TITLE: POG 8650 - National Wilm's Tumor Study - A POG Phase III Study

KEYWORDS: Wilm's tumor, renal tumor, nephroblastoma

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, A. COL MC; Crouch, G. LtCol MC; Hartman, K. LTC MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology Oncology

INITIAL APPROVAL DATE: 28 October 1986

New Anniversary Month: September

### STUDY OBJECTIVE

Gather data on morphology and correlate it with treatment and clinical outcome.

Refine clinical trials to reduce therapy to simpler and shorter regimens.

### TECHNICAL APPROACH

To attempt to give the usual five-day course in one day, (has been done with other tumors), and to examine in randomized trial with current therapies.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No new outcome analyses have been reported since the last COG Study Report from the Spring 2001 COG Meeting. This study closed to accrual effective 1 September 1994. Final accrual as of last reporting to POG (31 Jan 96) is 3335. There were a total of 14 patients registered at WRAMC; the last WRAMC registration was in July 1993. There were no unexpected toxicities reported. Of the 14 WRAMC registrants, 9 are followed at WRAMC and are in remission, 4 transferred to other COG institutions, and 1 died of relapse and progressive disease. Results showed no statistically significant difference in relapse-free survival or survival for patients treated with short versus long treatment regimens.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 14. The total number enrolled study-wide is 3335, multi-site study.

### CONCLUSIONS

Study should remain open for data collection for patients followed at WRAMC.

## DETAIL SUMMARY SHEET

TITLE: POG 8821 - Intensive Multi-agent Therapy vs. Autologous Bone Marrow Transplant Early in First CR for Children with Acute Myelocytic Leukemia - A Phase III Study

KEYWORDS: autologous bone marrow, transplant, acute myelocytic leukemia

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Crouch Gary LTC MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 27 September 1988

### STUDY OBJECTIVE

To: 1) determine DFS with intensive chemotherapy using non-cross resistant drug pairs; 2) determine if short-term intensive therapy with autologous bone marrow transplant (with 4-Hydroperoxycyclophosphamide purge) is effective therapy; and 3) compare the two regimens' results and to correlate outcome with clinical and laboratory features.

### TECHNICAL APPROACH

Registrants are 21 years of age and younger with previously untreated acute myelocytic leukemia (AML). Induction for both arms uses intrathecal Ara-C, daunomycin, Ara-C, 6-TG, followed by high-dose Ara-C. Patients are then randomized to receive IT Ara-C, VP-16/5-AZA plus ABMT with 4-HC purge, or to receive IT Ara-C, HDAC/daunomycin, Ara-C/6-TG, and VP-16/5-AZA.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study has been closed since 11 March 1993. The 666 group wide accrual figure remains unchanged. Of the seven patients registered on study at WRAMC, four relapsed (three of the relapsed patients died of their disease and one is in second remission after ABMT), one transferred to another COG institution, and two are alive (one in first CR and the other in CR2), off therapy. There have been no late reports of adverse reactions. Benefits to patients included the possibility of remission of disease. There have been no further reports from COG.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 7. The total number enrolled study-wide is 666 (multi-site study).

### CONCLUSIONS

Study should remain open to follow WRAMC registrants.

## DETAIL SUMMARY SHEET

TITLE: POG 8828 - Late Effects of Treatment of Hodgkin's Disease - A POG Non-therapeutic Study

KEYWORDS: childhood, Hodgkin's disease, long-term effects

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Hartman, Kip COL MC; Crouch, Gary LTC MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 23 May 1989

### STUDY OBJECTIVE

To estimate incidence of late effects following treatment for Hodgkin's disease on current frontline COG studies and to attempt to identify pre-treatment and/or on-treatment factors that predict high risk of specific late effects.

### TECHNICAL APPROACH

Registrants are patients on COG frontline Hodgkin's protocols and are followed through completion of late effects study forms every three years.

### PRIOR and CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study closed to patient accrual on 15 May 2002. There were no adverse effects from participation in this non-therapeutic study. Benefits to patients may result from greater awareness of late effects with subsequent earlier treatment intervention as a result of completing the late-effects study forms every three years.

Study coordinators attempted to assess late effects regarding cardiac, pulmonary, and endocrine/reproductive effects as well as second malignant neoplasms through responses to a late effects form designed for this purpose. While the overall response rate was high, at 461 responses, many of the responses were incomplete or the answer to a particular question was "unknown" so the coordinators will attempt to look at individual toxicity questions to see whether or not some questions may be answerable from the data available. No findings were available as of the 12 Feb 2003 Study Progress Report. [COG Study Progress Report, February 12, 2003]

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 9. The total number enrolled study-wide is 633, multi-site.

### CONCLUSIONS

Study should remain open to follow WRAMC registrants.

## DETAIL SUMMARY SHEET

TITLE: POG 9047 - Neuroblastoma Biology Protocol

KEYWORDS: Neuroblastoma, biology

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL, MC; Crouch, Gary LtCol

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 27 February 1990

NEW ANNIVERSARY DATE: 27 September 2003

### STUDY OBJECTIVE

To analyze cytogenetics of neuroblastoma cells and determine the clinical significance of genetic variations found, compared to conventional clinical, histologic, and biologic variables in predicting response to treatment or outcome. To develop a neuroblastoma serum and tissue bank for future studies, and to collect natural history and lab data on patients with untreated disease (stages A and DS).

### TECHNICAL APPROACH

All newly diagnosed patients 21 years old or less who are registered on POG neuroblastoma treatment protocols, or stage A or DS (favorable risk) will submit discarded biopsy material and serum for cytogenetic studies and banking.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This protocol, which closed to accrual on 5 April 2001 and was subsequently replaced by biology study ANBL00B1 (WU #01-66002; opened at WRAMC on 24 April 2001), is a biology study of all patients with neuroblastoma. The study collected the prognostic factors of INSS stage, age, MYCN copy number, ploidy, and Shimada histology upon which risk group assignment is based. A cell bank for future research is also maintained.

COG has not published a study progress report since the Fall 2001 report, which reported that 2,429 patients have been enrolled in the study and that there have been no reports of adverse events resulting from study participation. Benefits to patients included the possibility that the clinical significance of the genetic rearrangements more accurately predicted treatment outcome.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 15. The total number enrolled study-wide is 2429 (multi-site study).

### CONCLUSIONS

This study should remain open to follow WRAMC registrants.

## DETAIL SUMMARY SHEET

TITLE: POG 9233/34 - A Phase III Randomized Trial of Standard vs. Dose-Intensified Chemotherapy <3 years of Age with a CNS Malignancy Treated With or Without Radiation Therapy

KEYWORDS: brain tumor, child, pre-school, chemotherapy

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Hartman, Kip COL MC; Crouch, Gary LTC MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 26 May 1992

### STUDY OBJECTIVE

To study efficacy and toxicity of dose intensified chemotherapy in children less than three years old with selected types of brain tumors by means of a randomized comparison. To relate response to DNA index of tumor. To attempt to observe for disease progression over one year, with the option of giving irradiation if tumor relapses during this year.

### TECHNICAL APPROACH

Children less than three years of age with selected types of brain tumors will be randomized to receive either intensive or standard chemotherapy (POG 9233). If response is adequate, there will be one year of close observation, during which time radiation therapy on POG 9234 will be available if the tumor relapses. Patients who have less than adequate response on POG 9233 will receive irradiation on POG 9234 as soon as possible. The DNA index of diagnostic tumor tissue will be related to the treatment outcome.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

All strata for POG 9233 closed 8 May 1998; POG 9234 was closed on 14 December 14 2000. As of 27 Feb 2003, groupwide accrual on POG 9233 and POG 9234 was 338 and 54, respectively. WRAMC has four registrations: two have died of disease, and two remain in CR. A fifth patient was being followed at WRAMC after transferring from MAMC. This patient has since died from a secondary malignancy. Myelosuppression was the most common toxicity on POG 9233 (detailed toxicity data reported in last reported data, COG Study Progress Report, Spring 2001). Of the 164 eligible patients on POG 9233, Treatment 01/Regimen A/Control, 66 patients had a complete response and 57 patients had a partial response to treatment; while 89 patients out of the 166 eligible patients on Treatment 02/Regimen B/Test had a complete response and 47 had a partial response to treatment (detailed response data in current COG study report). Response data for patients on POG 9234 is masked. Five-year event free survival for eligible patients on treatment 01 is 19.1% (SE 4.3) and 22.3 (SE 4.6) for treatment 02. [Last reported data, COG Study Progress Report, Spring 2001] Benefits to patients include the possibility of remission of disease.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 4. The total number enrolled study-wide is 338 on POG 9233 and 54 on POG 9234 as of 27 Feb 2003, multi-site study.

### CONCLUSIONS

Study should remain open to follow study registrants at WRAMC.

## DETAIL SUMMARY SHEET

TITLE: POG 9317 - Chemotherapy for children with Advanced-Stage (III/IV) Diffuse Undifferentiated Burkitt's Lymphoma and B-Cell ALL: A Phase III Study

KEYWORDS: Burkitt's lymphoma, Cytosan, Ara-C

PRINCIPAL INVESTIGATOR: Edward, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Crouch, Gary LtCol

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 30 March 1993

### STUDY OBJECTIVE

1) To evaluate the efficacy of adding VP-16/ifosfamide intensification to the treatment of patients with advanced-stage B-cell malignancies: Stages III & IV DU NHL and B-cell ALL; 2) To compare the toxicity of high-dose Ara-C given by intermittent bolus (q 12 hrs x 4) vs. bolus/continuous infusion over 48 hours.

### TECHNICAL APPROACH

Registrants must be 21 years old or younger and have had no previous chemotherapy. Concomitant registration on POG 9400 (biology study) is required. Children with diagnosed advanced-stage (III-IV) diffuse undifferentiated Burkitt's lymphoma and B-cell ALL will receive randomized induction therapy to compare the toxicity of high-dose Ara-C given by intermittent bolus (q 12 hours x 4) vs. bolus/continuous infusion over 48 hours, followed by randomization to receive or not receive VP/IFOS for intensification.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study closed to accrual 23 March 1999. The total number of subjects enrolled study-wide is 343. The total number enrolled since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. Of the 2 patients enrolled at WRAMC, 1 died of progressive disease after relapse and 1 is alive and remains in CR. There have been no published study reports since COG's Spring 2001 Report of Studies, which published no significant difference in event-free survival between ARA-C vs. ARA-C+VP/IFOS, and continuous infusion vs. bolus ARA-C. The following is of note: For the combined group of B-ALL CNS + patients and Stage IV CNS + patients, 2-year EFS plateaued around 79% and few CNS relapses have been reported in any of the disease strata. These last two observations suggest that the 9317 treatments are excellent for both CNS prophylaxis and for the treatment of CNS disease (at diagnosis). Group-wide reported ADRs and all toxicities are listed in the COG Spring 2001 Report of Studies. There has been significant absolute neutrophil count, platelet and hemoglobin toxicity as expected for this therapy. Benefits to patients include the possibility of remission of disease.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 343, multi-site study.

### CONCLUSIONS

Study should remain open to follow WRAMC registrant.

## DETAIL SUMMARY SHEET

TITLE: POG 9351/CCG 7921 - Trial of Doxorubicin, Cisplatin and Methotrexate with and without Ifosfamide, with and without Muramyl Tripeptide Phosphatidyl Ethanolamine (MTP-PE) for Treatment of Osteogenic Sarcoma

KEYWORDS: doxorubicin, osteogenic, sarcoma

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Crouch, Gary LtCol MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 22 February 1994

### STUDY OBJECTIVE

To: 1) improve survival and compare results of two chemotherapeutic regimens; 2) determine whether histologic response assessed after prolonged therapy with more drugs predicts disease-free survival (DFS) with the same power seen in CCG-782, which used fewer drugs over a shorter time; 3) determine whether liposomal muramyl tripeptide-phosphatidyl ethanolamine can improve DFS; and 4) determine whether MDR expression is useful to determine prognosis or assign therapy.

### TECHNICAL APPROACH

Patients  $\leq$  30 years old will be treated in a Phase III randomized trial of two chemotherapy regimens for the treatment of newly diagnosed, previously untreated osteogenic sarcoma. One regimen calls for the administration of high-dose methotrexate, doxorubicin, and cisplatin. The other regimen calls for the administration of these agents plus ifosfamide. Chemotherapy is administered for 10 weeks prior to surgical resection of primary tumor and any metastatic disease. Patients also are randomly assigned either to receive MTP-PE with maintenance chemotherapy or to receive maintenance chemotherapy alone.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This protocol was closed to accrual on 25 November 1997. There were eight toxic deaths on this study: five due to infections during neutropenia, one an intraoperative mortality, and there is insufficient data to characterize the other two. Results to date show no difference in outcome due to MTP in the CDDP/DOX/HDMTX regimen (4yr EFS=65% w/o MTP vs. 62% w/ MTP). There does appear to be a difference in outcome with the four-drug regimen (above combination plus ifosfamide) when MTP was added (4yr EFS= 57% without MTP vs. 70% with MTP). A detailed discussion of results and toxicity appears in the reference cited below. There have been no toxic deaths at WRAMC. Three of the four WRAMC registrants have died of recurrent or progressive disease. The other WRAMC registrant is alive with no evidence of disease. Benefits to patients include the possibility of remission of their disease. [Data is from Spring 2002 COG Current Report of Studies]

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 4. The total number enrolled study-wide is 679 (POG 321), if multi-site study.

### CONCLUSIONS

Study is closed to accrual. Study should remain open to follow WRAMC registrant.



## DETAIL SUMMARY SHEET

TITLE: POG 9405 - ALinC16; Protocol for Patients with Newly Diagnosed Standard-Risk Acute Lymphoblastic Leukemia - POG Phase III Study

KEYWORDS: leukemia, lymphoblastic, children

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC

ASSOCIATES: Mosijczuk, Askold COL MC; Crouch, Gary LTC MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 20 December 1994

### STUDY OBJECTIVE

To: 1) determine the efficacy of a higher vs. standard dose MTX infusion during consolidation; 2) describe the incidence of adverse reactions occurring with administration of higher dose MTS; 3) determine the efficacy of delivering oral 6 MP on a once vs. twice daily schedule during continuation.

### TECHNICAL APPROACH

Newly diagnosed B-Precursor ALL patients (including B-ALL that is not L3 morphology) will be enrolled after registration on POG 9400. Patients will be randomized to compare the efficacy of a higher vs. standard dose MTX infusion during consolidation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study was closed to accrual in December 26, 1995 due to excessive acute neurotoxicity. A total of 299 patients were registered on the protocol group wide, with 285 non-Down patients achieving remission. One patient has been registered at WRAMC and continues to do well in complete remission without evidence of neurotoxicity. Reported toxicity was similar to that seen historically with methotrexate, including slurred speech, staring, ataxia and other gross motor findings, behavioral disorders, seizures, somnolence, and loss of milestones. Of concern was that, if actuarial projections continued, the incidence of neurotoxicity would approach 30%, compared with 3-12% historically. The protocol therapy was amended in January 1996 to minimize the risk of CNS toxicity in patients already enrolled and was closed early due to predicted neurotoxicity in the protocol. The last report from COG (Joint POG/CCG Fall 1999 Meeting Agenda and Current Report of Studies) was restricted to reporting of CNS toxicity. Of the 285 patients, 70 (25%) had a reportable CNS adverse event; 29 (10%) were seizures. Benefits to patients included the possibility of remission of disease.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 301, multi-site, as of 29 Oct 02.

### CONCLUSIONS

Study should remain open to follow the one, WRAMC registrant.

## DETAIL SUMMARY SHEET

TITLE: POG 9406 - ALinC16; Protocol for Patients with Newly Diagnosed High-Risk Acute Lymphoblastic Leukemia - A POG Phase III Study

KEYWORDS: Newly diagnosed, high-risk, lymphoblastic leukemia

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Crouch, Gary LtCol MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 20 December 1994

### STUDY OBJECTIVE

To: 1) compare, in a randomized trial, the efficacy and toxicity of 12 intensive courses of IV MTX/6-MP vs. 12 intensive courses of alternating chemotherapy pairs; and 2) assess short-term toxicity of modified regimen B (Treatment C) where higher-dose MTX is substituted in first cycle of consolidation.

### TECHNICAL APPROACH

Newly diagnosed non-T, non-B ALL patients who fit the following criteria will be enrolled: 1-21 years old, poor prognostic features based on age, ploidy, translocations, and immunophenotypes, and with no history of prior treatment. Two treatments will be compared: 12 intensive courses of IV MTX/6MP vs. 12 intensive courses of alternating chemotherapy pairs (MTX/6-MP, VM-26/Ara-C, daunomycin/Ara-C).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study was closed to accrual on 11/15/1999 having met its accrual goals. Final accrual is 910 group wide. Total registrations at WRAMC remains at three. All 3 WRAMC patients are in CR. The most significant toxicity has been neurotoxicity, which resulted in an amendment to the protocol adding additional leucovorin and changing triple intrathecal chemotherapy to methotrexate alone. No adverse reactions at WRAMC since the last report. Four-year event free survival of randomized subjects is 74% (SE 2%); see enclosed table. [COG Study Progress Reports Fall 2002.] Benefits to patients included the possibility of disease remission.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 3. The total number enrolled study-wide is 910, multi-site, as of 29 Oct 02.

### CONCLUSIONS

Study should remain open to follow WRAMC registrants.

## DETAIL SUMMARY SHEET

TITLE: POG 9362 - A Phase II Study of Alpha Interferon in HIV-Related Malignancies; A Pediatric Oncology Group Wide Study

KEYWORDS: interferon, HIV, malignancies

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Crouch, Gary LTC MC

DEPARTMENT: Pediatrics

STATUS: C

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 28 March 1995

### STUDY OBJECTIVE

(1) Estimate the complete response rate for HIV-related malignancies treated with alpha interferon; 2) estimate the 1-year disease-free survival; and 3) evaluate the toxicity of alpha interferon alone or in combination with anti-retroviral therapy.

### TECHNICAL APPROACH

All patients are required enroll in POG 9182, and in compliance with all specimen submission requirements of that protocol. Additional tissue sampling will be minimized, including CSF or blood sampling except as required for monitoring for toxicity and tumor response. HIV-positive children with refractory or newly diagnosed malignancies will be treated with alpha IFN alone or in combination with other antiretroviral agents.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study closed to patient entry on 1 July 2002 due to poor accrual. As of 20 January 2003, 9 subjects were enrolled on this study; no subjects were enrolled at WRAMC. No study progress reports have been published since the COG Spring 2001 report, at which time response was still masked and toxicity was minimal.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 9, multi-site study.

### CONCLUSIONS

Because there are no WRAMC registrants and this study has closed to patient accrual, this study should be marked 'Complete' at WRAMC.

## DETAIL SUMMARY SHEET

TITLE: POG 9421 - Phase III Evaluation of Standard vs. High-Dos Ara-C Induction Followed by the Randomized Use of Cyclosporin A as an MDR Reversal Agent Compared to Allogeneic BMT in Childhood AML

KEYWORDS: allogeneic, BMT, AML

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Crouch, Gary LtCol; Merino, Margret MAJ; Reddoch, Shirley MD

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 28 March 1995

### STUDY OBJECTIVE

- (1) To determine the effect of high-dose vs. standard-dose Ara-C induction on complete response (CR) and event-free survival (EFS) in childhood AML
- (2) Compare the EFS in childhood AML after three cycles of consolidation with or without the multi-drug resistance (MDR) modulator cyclosporin A.
- (3) Compare the EFS between patients genetically randomized between allogeneic BMT and chemotherapy.

### TECHNICAL APPROACH

To test, in a randomized study, the role of HD Ara-C in military health care beneficiaries who are <21 years of age, presenting with newly-diagnose acute myeloid leukemia who have had no prior therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study was closed to accrual on 15 August 1999. Final accrual was 654 subjects group wide. Of those, 624 were evaluable. There were no new registrations at WRAMC since the last APR, leaving the total registrations at 5. Two of these patients are still being followed at WRAMC and are in CR; 2 have been transferred to other military COG institutions; 1 patient registered at WRAMC died of progressive disease after a BMT in first CR. A patient was accepted in transfer from another COG institution in 1996 and follow up data was submitted to COG until the patient's death from infection in 1998. No new study reports have been published since the COG Fall 2001 Report of Studies which reported the following: Of the 624 evaluable patients, 559 (89.6%) entered remission (530 had M1 marrow and 29 had M2a marrow). Death accounted for 18 of the 65 induction failures (27.6%); the other 48 patients who failed to enter remission had resistant disease. The remission rate for 57 Down syndrome patients was 54/57 (94.7%). The remission rate for patients who received induction of DAT was 250/286 (87.4%), similar to the remission rate of 255/281 (90.7%) for patients who received induction of HDAT ( $p=0.10$ ). The mean ( $\pm$ SE) rates of event-free and overall survival three years after randomization were  $41.2 \pm 2.8\%$  and  $55.6 \pm 2.7\%$ , respectively. There was no statistical difference in remission rate, OS or EFS between non-BMT groups. The estimated rates of remission duration for patients who received Allogeneic BMT ( $N=83$ ) and for all other patients ( $N=422$ ) were  $67.2 \pm 7.3\%$  and  $37.2 \pm 3.3\%$ , respectively. Myelotoxicity has been significant but as anticipated. ADRs and toxicity details are listed in COG's Fall 2001 Report of Studies, October 2001. Benefits to patients include the possibility of remission of disease.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 6. The total number enrolled study-wide is 654, multi-site study.

### CONCLUSIONS

Study should remain open to follow WRAMC registrants.

## DETAIL SUMMARY SHEET

TITLE: POG 9201 ALinC16 - Treatment for Patients with Lesser Risk Acute Lymphoblastic Leukemia - A Pediatric Phase III Study

KEYWORDS: acute, lymphoblastic, leukemia

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Hartman, Kip COL MC; Crouch, Gary LTC MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 23 May 1995

### STUDY OBJECTIVE

- 1) Confirm the outstanding results in patients with lesser-risk non-T, non-B acute lymphoblastic leukemia (ALL) treated in a fashion similar to the least intensive arm of POG 8602 (ALinC 14, Arm A).
- 2) Study laboratory correlates from POG 9400 and clinical correlates with outcome in pooling studies 9201, 9405, and 9406.

### TECHNICAL APPROACH

Military health care beneficiaries who are  $\leq 21$  years of age with newly-diagnosed ALL will be prospectively identified to be at lowest risk of treatment failure based on the new consensus risk groups and through the use of trisomies 4 and 10 in a trial to confirm the very favorable results of ALinC #14.

### PRIOR and CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study was closed to accrual on 15 Nov 1999 with a final group-wide accrual on the phase III portion of this study of 625. There are four WRAMC registrants. Of the four registrants, one died of disease after bone marrow transplantation at another institution; two are in CR; and one transferred to another COG institute but has since returned to WRAMC for continuation of routine follow up. (The other institute is still responsible, however, for submitting the patient's COG data). WRAMC has accepted two transfer patients on protocol from other COG institutions. Both are in CR.

There are no reports of adverse events at WRAMC. Among the 622 eligible Phase III patients, there have been 87 Adverse Events and Reported Toxicities (including 33 CNS [10 seizures], 40 liver/liver function) - see the attached list of group wide Phase II. Group wide, there have been three induction deaths among the 622 eligible Phase III patients: two from sepsis and one attributed to pancreatitis on autopsy. Aside from the three induction deaths, all patients achieved remission. Event-free survival at four years is 90% (SE=1.4%) and at 5 years it is 87% (SE=2.1%). [COG Study Progress Report, Spring 2003.] Benefits to patients include the possibility of remission of disease.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 4. The total number enrolled study-wide is 625, multi-site study.

### CONCLUSIONS

The study should remain open to follow WRAMC's study registrants.

## DETAIL SUMMARY SHEET

TITLE: POG 9354/CCG 7932 - Phase III Evaluation of Intensified Vincristine, Doxorubicin, Cyclophosphamide, Ifosfamide, and Etoposide in the Treatment of Newly-Diagnosed Ewing's Sarcoma or Primitive Neuroectodermal Tumor of Bone or Soft Tissue

KEYWORDS: newly-diagnosed, Ewing's sarcoma

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Hartman, Kip COL MC; Crouch, Gary LTC MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 29 August 1995

### STUDY OBJECTIVE

To compare the event-free survival, and toxicity in patients with Ewing's sarcoma treated with a 48-week course of standard-dose vincristine, doxorubicin, cyclophosphamide, ifosfamide, MESNA, and etoposide plus G-CSF with that of patients treated with the same agents given in a 30-week dose-intensified regimen.

### TECHNICAL APPROACH

Patients less than or equal to 30 years of age with newly-diagnosed Ewing's sarcoma or PNET of bone or soft tissue will be randomized to receive either the 48-week course of standard-dose vincristine, doxorubicin cyclophosphamide, MESNA and etoposide plus G-CSF, or the 30-week dose-intensified regimen using the same agents.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study was closed to accrual on 9/15/98. There were 492 group wide registrations. Three patients have been registered at WRAMC. Of those three, one was officially transferred to another COG institution, one transferred to another Military health care institution but WRAMC is still responsible for COG data submission, and one is still followed at WRAMC. The two patients for whom WRAMC is still responsible for COG data submission are alive in remission.

A Current Report of Studies has not been published by COG since the Fall 2001 Report, which contained the following data: Mucositis and grade 4 hematologic toxicity was more common on Regimen B than Regimen A; there was a total of seven toxic deaths, four on Regimen A - two of the seven were due to post-surgical complications. Adverse drug reactions were reported as being equally distributed between the two regimens. Secondary leukemia was reported in nine patients (five on Regimen A and four on Regimen B). The incidence of secondary leukemia was reported as being no greater than that reported in previous studies. Response was reported as follows: Regimen A, 72.2% (CR 2.4%; PR 69.8%); Regimen B, 78.7% (CR 3.5%; PR 75.2%). Overall event-free survival and survival were reported as 74.7 (SE 2.4) and 83.0 (SE 2.1), respectively, at 3 years.

Benefits to patients include the possibility of remission of disease.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 3. The total number enrolled study-wide is 492, multi-site study.

### CONCLUSIONS

Study should remain open at WRAMC to follow WRAMC registrants.

## DETAIL SUMMARY SHEET

TITLE: An Overview of the Research Protocol Entitled POG 9440/CCG 494 - National Wilms' Tumor Study – 5 - Therapeutic Trial and Biology Study

KEYWORDS: Wilms', therapeutic, biology

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Crouch, Gary LTC MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 26 September 1995

### STUDY OBJECTIVE

1) Increase the survival rate of children with favorable Wilms' tumor and other renal tumors of childhood; 2) determine if loss of heterozygosity (LOH) for chromosome 16q markers in tumor tissue is associated with a poorer diagnosis for children with favorable histology Wilms' tumor; and 3) determine if loss of heterozygosity for chromosome 1p markers in tumor tissue is associated with a poorer prognosis for children with favorable histology Wilms' tumor.

### TECHNICAL APPROACH

Pediatric military health care beneficiaries will be registered as either studied, followed, or registered only. Study patients must be less than 16 years of age, not received chemotherapy or radiation therapy, and have a stage I-IV favorable histology Wilms' tumor, stage I-V focal or diffuse anaplastic Wilms' tumor stage I-V clear-cell sarcoma of the kidney or stage I-V rhabdoid tumor of the kidney. Patients must have undergone a nephrectomy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study was closed to accrual on 1 June 2002. The total number of registrants study wide is 2853. There are eight WRAMC registrants. Of the eight WRAMC registrants, two have transferred to other COG institutions, leaving six registrants still followed by WRAMC. There have been no adverse events at WRAMC and none reported by COG. Benefits to patients include the possibility of remission of disease.

Patients with stage I favorable histology (FH) Wilms' tumor < 550 grams, who are <24 months of age have an 87% 2 year relapse free survival (RFS) and 100% survival following nephrectomy only as initial therapy; while patients with stage I diffuse anaplasia have unexpectedly low 2 year RFS at 76.7%, and stage IV and V patients continue to have less than excellent outcome at 68 and 63% 2 year RFS, respectively. Stage I CCSK patients, 10 in number, currently have 100% 2 year RFS after treatment with regimen I. Patients with stage II/III diffuse anaplasia at 64% and stage IV at 24% appear not to be doing better on regimen I compared with regimen DD4A. NWTS-5 therapy was found to be ineffective for Stage IV diffuse anaplastic Wilms' tumor and all stages of rhabdoid tumor. [Renal Tumor Committee Minutes, Fall 2002]

The most current data from NWTS-5 on LOH at chromosomes 1p and 16q reports that the LOH for chromosome 1p was associated with higher risk of recurrence for patients with stages I or II FH disease, but not for patients with stages III or IV FH disease; while LOH at 16q was associated with higher risk of recurrence for patients with stages I or II FH disease, but the risk and statistical significance were not as great as for LOH at 1p. The risk of recurrence was greatest for patients with LOH at both 1p and 16q; this risk was significant for patients with stages I/II disease and III/IV disease. [Renal Tumor Committee Minutes, Spring 2003]

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 8. The total number enrolled study-wide is 2853, multi-site study.

### CONCLUSIONS

Study should remain open to follow WRAMC registrants.

## DETAIL SUMMARY SHEET

TITLE: Support of Pediatric Oncology Group Activities, WRAMC

KEYWORDS: cancer, grant, children

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Crouch, Gary LTC MC, Merino, Margret MAJ MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 30 January 1996  
Umbrella Study

### STUDY OBJECTIVE

The NIH grant application is to bring in the funds in support of the research conducted at WRAMC sponsored by the Children's Oncology Group (formerly Pediatric Oncology Group). These funds are distributed through the Geneva Foundation.

### TECHNICAL APPROACH

None.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Please refer to individual COG/POG protocols.

### CONCLUSIONS

None.



## DETAIL SUMMARY SHEET

**TITLE:** A Multicenter Study to Determine the Prevalence and Clinical Characteristics of Barrett's Esophagus in Childhood

**KEYWORDS:** Barrett's Esophagus, esophagitis, gastroesophageal reflux

**PRINCIPAL INVESTIGATOR:** COL Philip L. Rogers MC  
**ASSOCIATES:**

**DEPARTMENT:** Pediatrics  
**SERVICE:** Pediatric GI & Nutrition

**STATUS:** O  
**INITIAL APPROVAL DATE:** 28 May 1996

### STUDY OBJECTIVE

To determine the prevalence of short segment Barrett's esophagus in pediatric patients presenting for esophagogastroduodenoscopy (EGD); 2) describe the clinical and histologic findings in patients with Barrett's esophagus; 3) correlate the clinical and histologic findings in patients with reflux esophagitis; and 4) validate the use of a gastroesophageal reflux questionnaire in the evaluation of gastroesophageal reflux disease in children.

### TECHNICAL APPROACH

The study population will consist of 650 patients consecutively enrolled who are scheduled for routine EGD by the division of Pediatric Gastroenterology and Nutrition at WRAMC and other participating centers. A gastroesophageal reflux questionnaire will be completed prior to the performance of an EGD. A standard EGD with biopsies will be performed. Additionally, a biopsy at the squamocolumnar junction will be obtained. The histologic characteristics of the esophageal biopsies and prevalence of SSBE will be determined. The clinical presentations of the patients, as determined by the questionnaires, will be compared to the histologic findings. The ability to determine esophagitis by the use of questionnaires will be determined.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study is closed for patient enrollment since the last summary. The data is still being reworked in preparation for submission in the next few months. There is a significant amount of patient questionnaire information that has yet to be analyzed, but this will be completed in the next six months when it is anticipated that this study will be closed.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 307. The total number enrolled study-wide is 307, if multi-site study.

### CONCLUSIONS

The prevalence of Barrett's esophagus in childhood is very low, but changes in esophageal epithelial lining consistent with dysplasia can be demonstrated if tissue biopsies are carefully evaluated. In our study, two patients with possible BE had a significant history for gastroesophageal reflux. Our paper presents important descriptive data about Barrett's esophagus and highlights the fact that BE is rare in children but can be present. However, careful screening and biopsy evaluation is required. Our data suggests that biopsies at the squamocolumnar junction (SCJ) may be more revealing about GERD in children than the standard biopsies taken at 3-5 cm above the SCJ. This data requires further analysis as does patient questionnaire information that we believe helps to define the population that requires more intensive and careful screening for Barrett's esophagus.

## DETAIL SUMMARY SHEET

TITLE: POG 9605 - ALinC 16 Protocol for Patients with Newly-Diagnosed Standard-Risk Acute Lymphoblastic Leukemia (ALL)

KEYWORDS: pediatrics, lymphoblastic, leukemia

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Hartman, Kip COL MC; Crouch, Gary LTC MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 25 June 1996

### STUDY OBJECTIVE

1) Determine if EFS can be improved with the addition of six months of delayed intensification with divided-dose oral methotrexate plus oral 6 MP as divided, or once a day dose given during intensification and continuation; 2) correlate laboratory and clinical findings from this study, and POG #s 9400, 9201, and 9406; 3) assess significance of marrow findings after two weeks of induction; and 4) describe occurrence and prognostic significance of elevated transaminases

### TECHNICAL APPROACH

After induction and consolidation, patients were randomized to one of four late intensification/consolidation arms. Regimen 1: Weekly IM MTX plus once daily oral 6MP intensification followed by daily oral 6MP in continuation. Regimen 2: Divided dose oral MTX plus once daily oral 6MP intensification followed by daily oral 6MP in continuation. Regimen 3: Weekly IM MTX plus divided-dose oral 6MP intensification followed by divided-dose 6MP in continuation. Regimen 4: Divided-dose oral MTX plus divided-dose oral 6MP intensification followed by divided-dose 6MP continuation. All patients received vincristine/prednisone pulses and IT MTX/Ara-C/HC during continuation therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study closed to accrual on 15 November 1999. Final group wide accrual is 1,087. WRAMC has three registrants. Of the three registrants, two are in complete remission and one transferred to another COG institution. WRAMC accepted two transfers from other COG institutions. Of the two transfers, one subsequently transferred to another COG institution and one, who was removed from study because of bone marrow relapse, died from his disease. Four year event-free survival is 80% (SE=1.8%) and 80% (SE=5.7%) for the standard prognosis and poor prognosis patients, respectively. There have been no ADRs at WRAMC. Group wide, there have been 166 reported CNS ADRs in 158 patients (75 seizures in 70 patients). By arm, there have been 52 (23 seizures) on A; 33 (13 seizures) on B; 37 (19 seizures) on C, and 44 (20 seizures) on D. The distribution of events was Induction 8 (5 seizures), Consolidation 72 (26 seizures), and Maintenance 85 (43 seizures). Observed rates for CNS events were 6.8% by the end of consolidation and 14.8% by the end of therapy. Observed rates for seizures were 2.4% by the end of consolidation and 6.5% by the end of therapy. [COG Study 9605 Progress Report, Spring 2003]

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 3. The total number enrolled study-wide is 1087, multi-site study.

### CONCLUSIONS

Study should remain open to follow WRAMC registrants.

## DETAIL SUMMARY SHEET

TITLE: POG 9404 - T-Cell #4 Protocol - Intensive Treatment for T-Cell Acute Lymphoblastic Leukemia and Advanced-Stage Lymphoblastic Non-Hodgkin's Lymphoma

KEYWORDS: leukemia, T-Cell, chemotherapy

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Hartman, Kip LTC MC; Crouch, Gary LtCol MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 27 August 1996

### STUDY OBJECTIVE

1) Determine, in a randomized trial, the effectiveness of high-dose methotrexate (HD MTX) when added to a multi-agent chemotherapy backbone (DFC1 87-001) proven effective in T-Cell acute lymphoblastic leukemias (T-all); 2) determine, in a randomized trial, the role of the cardioprotectant Zinecard (DZR) in preventing cardiotoxicity; and 3) study the biology of T-Cell lymphoid malignancies, including the correlation of minimal residual disease with event-free survival, utilizing the TAL 1 proto-oncogene, p53 and p16 tumor suppressor genes, and drug sensitivity profiles of blast cells to adriamycin, methotrexate, and cytarabine.

### TECHNICAL APPROACH

Patients with T-ALL (DR-T+) who are <22 years old, and patients with lymphoblastic lymphoma Murphy stage III or IV who are <21 years old (including those <12 months) will be randomized to receive or not receive high-dose methotrexate and Zinecard. Response rates and degree of anthracycline cardiotoxicity will be evaluated and compared.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study closed to accrual on 10 Sep 2001. A total of 573 patients were accrued - 541 eligible. There have been three WRAMC registrations. All three WRAMC registrants are doing well in complete remission. Group-wide patient characteristics are T-ALL: 366 (68%) and Lymphoblastic NHL: 175 (32%).

In September 2000, the methotrexate randomization was terminated due to a positive efficacy and subsequently all patients are receiving high dose MTX (HDM). Analysis of outcomes in the first 441 patients as of September 2000 demonstrated improved EFS for patients treated on the HDM arm (72.2% in 221 patients in No HDM group vs. 86.0% in 220 patients in HDM group). Toxicity was the same in both treatment arms except for an increased incidence of severe Grade 3 or 4 mucositis in patients receiving the HDM. There have been 148 patients reporting ADRs to date. Seventy-eight involved the CNS, including 28 seizures. Some of the neurotoxicity can be attributed to specific drug effect such as Vincristine peripheral neuropathy, asparaginase-related CNS thrombosis, or prednisone behavioral disturbances and are not included as true CNS events. [COG's Study Progress Report Spring 2003] Benefits to patients include the possibility of remission of disease.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 3. The total number enrolled study-wide is 573, multi-site study.

### CONCLUSIONS

Study should remain open to follow WRAMC registrants.

## DETAIL SUMMARY SHEET

TITLE: Bone Mineral Density in Survivors of Childhood Thyroid Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Powers, Patricia COL MC

ASSOCIATES:

DEPARTMENT: Pediatrics

SERVICE: Pediatric Endocrinology

STATUS: O

INITIAL APPROVAL DATE: 27 April 1999

### STUDY OBJECTIVE

This is a pilot observational study evaluating bone mineral density of patients diagnosed with thyroid cancer at <21 years of age.

### TECHNICAL APPROACH

Potential subjects are identified from pre-existing databases of pts diagnosed with thyroid cancer in childhood (databases are under WU #6398 and #6414). After obtaining consent, subjects complete a questionnaire (re: demographics, treatment and status of thyroid cancer, other medical problems, exercise habits, calcium intake, age at puberty, and, for females, menstrual history) and undergo a DEXA scan. In addition, subjects' medical records are reviewed.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 3. There have been no adverse events and no subjects have withdrawn from the study.

### CONCLUSIONS

No progress was made on this study in the past year. My goal this year is to work closely with the Adult Endocrinology Service to identify and efficiently recruit eligible subjects for this study.

## DETAIL SUMMARY SHEET

TITLE: Defense and Veterans Head Injury Program (DVHIP) - WRAMC Core Evaluation Protocol

KEYWORDS: traumatic brain injury, head injury

PRINCIPAL INVESTIGATOR: Deborah L. Warden, MD

DEPARTMENT: Neurology

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 31 August 1993

### STUDY OBJECTIVE

To ensure that all military and DVA traumatic brain injured (TBI) patients receive TBI-specific evaluation and follow-up, while at the same time collecting standardized patient outcome data that will allow us to evaluate the relative efficacy and cost of various TBI treatment and rehabilitation strategies, and to define optimal care for individuals with TBI.

### TECHNICAL APPROACH

Patients are generally referred to the TBI program directly from CONUS and OCONUS sites or from the departments of neurology, neurosurgery, rehabilitation medicine, or general/orthopedic surgery. The current standard of care for TBI patients at WRAMC consists of a three to four day evaluation. The evaluation is generally completed through outpatient visits. However, some patients may need a longer period in the hospital for treatment purposes. The evaluation can be completed on an in-patient basis in such situations. In most cases, however, the intent of the evaluation program is to return patients promptly to the referring facility, or, when possible and clinically indicated, to a designated TBI treatment close to their home. A dedicated TBI case manager/discharge planner in our program facilitates this disposition process. We generally conduct standard of care evaluations on three to five patients per week. On average, we have provided baseline evaluations for between 65 and 85 patients per year. Each patient receives neurological, neuropsychological exams, psychiatric examinations; EEG, and other testing as clinically indicated. Following the comprehensive evaluation, patients are returned to duty and followed. No significant changes have been made to the evaluation procedure over the past year.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The Core Evaluation Protocol remains active as we continue to enroll patients and provide follow-up evaluations for enrolled patients over 24 months. As of 2 July 2003, 505 patients have been enrolled in the protocol and have received baseline evaluations. This year 85 subjects received baseline evaluations and 43 follow-up evaluations were completed. There have been 3 adverse events reported over the last year - none directly attributable to the protocol. No patients withdrew from the study this year.

Based on DCI guidance, an addendum was submitted on 9 April 2003 requesting that the consent form for the family member/friend be discontinued because these individuals are not subjects of the study nor are they secondary subjects. Their information is being obtained only to confirm information about the study participant's functioning both before and after injury. Per the HUC meeting on 10 June 2003, we will be developing an alternate consent procedure and an informational paragraph to be used as an alternate consent for the family member/friend. These changes will not be incorporated until final written approval is obtained from DCI. The number of subjects enrolled to the study since last APR at WRAMC is 85, and the total enrolled to date at WRAMC is 505.

### CONCLUSIONS

We are submitting an "Exception to Policy" concurrent with this APR requesting extension of this protocol until HUC review and approval of the new protocol. A new protocol was submitted to DCI and was reviewed by CIC on 17 June. Upon final approval of the new protocol, this protocol will be closed.

## DETAIL SUMMARY SHEET

**TITLE:** An Open Label Study of Interferon Beta-la (Recombinant Human Interferon Beta) in Subjects with Multiple Sclerosis (Biogen Protocol Number, C94-801-P, Version 6) updated 20 January 1999.

**KEYWORDS:** multiple sclerosis, interferon, Beta-la

**PRINCIPAL INVESTIGATOR:** Robert J. Labutta LTC MC

**ASSOCIATES:** Edward S. Urban, COL (ret), MC, USA, Judith A. Brooks RN MSN CCRC

**DEPARTMENT:** Neurology

**STATUS:** C

**SERVICE:**

**INITIAL APPROVAL DATE:** 25 April 1995

### STUDY OBJECTIVE

To obtain safety information regarding the use of repeated IFN-B-la dosing in subjects with multiple sclerosis.

### TECHNICAL APPROACH

Patients will be administered 30 micrograms of IFN-B-la intramuscularly once a week for six years.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0. The total enrolled to date at WRAMC is 30. The total number enrolled study-wide is 382.

Serious adverse events from WRAMC and other sites have been reported as they occurred. During the final monitoring visit, we were unable to find documentation of IRB notification for four WRAMC SAEs. They have been forwarded to DCI. Pharmacy has been notified of the completion of this study. The last study drug was dispensed in August 2001. All remaining study drug was destroyed in May 2002 according to policy.

### CONCLUSIONS

Participation in multi-center Multiple Sclerosis trials can be successfully accomplished at WRAMC. Treatment of Multiple Sclerosis with interferon beta has long-term safety and efficacy. We will retain the regulatory documents and the subjects' study records in the Department of Neurology for at least fifteen years following the closure of this study.

## DETAIL SUMMARY SHEET

**TITLE:** An Open Label Uncontrolled Trial of Long-Term Treatment with Poly-ICLC in Patients with Malignant Gliomas and Multiple Sclerosis.

**KEYWORDS:** poly-ICLC, glioma, multiple sclerosis

**PRINCIPAL INVESTIGATOR:** Askold D. Mosijczuk COL MC  
**ASSOCIATES:**

**DEPARTMENT:** Pediatrics

**STATUS:** O

**SERVICE:** Pediatric Hematology-Oncology

**INITIAL APPROVAL DATE:** 23 April 1996

### STUDY OBJECTIVE

To maintain treatment and follow up of patients on intramuscular Poly-ICLC for multiple sclerosis and malignant glioma.

### TECHNICAL APPROACH

Malignant glioma patients were administered Poly-ICLC at 20 mcg/kg three times a week for 36 months and then tapered. The multiple sclerosis patients were receiving between 0.5-10 mg once or twice a week. They have all discontinued treatment as of December 2001.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 15. The total number enrolled study-wide is N/A. No adverse events have been reported. Currently there is only one patient who is receiving Poly ICLC 20 micrograms/kg IM twice weekly. This is a 14-year-old female with progressive but stable Anaplastic astrocytoma of the right temporal lobe diagnosed in 1992. Patient failed prior chemotherapy, surgery and radiation, and was begun on Poly-ICLC in 1993 on a compassionate basis on this protocol. Patient was already in a vegetative state at start of Poly-ICLC, and remains so to this day. There continues to be no hematologic or other toxicity present to this medication. Per telephonic discussion with initial PI of this study, all glioma patients are off Poly-ICLC for several years, with "5 or 6" of the initial 13 patients treated with Poly-ICLC still doing well 8-12 years later. Per telephonic discussion with PI of a phase II study of Poly-ICLC in children with recurrent malignant and low-grade gliomas treated at Children's National Medical Center in Washington, DC, one patient with malignant glioma completed Poly-ICLC three years ago and is "doing well," and two other children with grade II (low-grade) glioma are also two years off therapy and "doing well." Results are not published, and additional details are not available to me.

### CONCLUSIONS

All MS patients have transitioned to one of the FDA approved Multiple Sclerosis medications. One glioma patient is still on Poly-ICLC on a compassionate use basis. Askold D. Mosijczuk COL MC is the current PI.

## DETAIL SUMMARY SHEET

**TITLE:** An Open Label Uncontrolled Trial of Long-Term Treatment with Poly-ICLC in Patients with Malignant Gliomas and Multiple Sclerosis.

**KEYWORDS:** poly-ICLC, glioma, multiple sclerosis

**PRINCIPAL INVESTIGATOR:** Askold D. Mosijczuk COL MC  
**ASSOCIATES:**

**DEPARTMENT:** Pediatrics

**STATUS:** C

**SERVICE:** Pediatric Hematology-Oncology

**INITIAL APPROVAL DATE:** 23 April 1996

### STUDY OBJECTIVE

To maintain treatment and follow up of patients on intramuscular Poly-ICLC for multiple sclerosis and malignant glioma.

### TECHNICAL APPROACH

Malignant glioma patients were administered Poly-ICLC at 20 mcg/kg three times a week for 36 months and then tapered. The multiple sclerosis patients were receiving between 0.5-10 mg once or twice a week. They have all discontinued treatment as of December 2001.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 15. The total number enrolled study-wide is N/A. No adverse events have been reported. Currently there was only one patient receiving Poly ICLC 20 micrograms/kg IM twice weekly. This was a 14-year-old female with progressive but stable anaplastic astrocytoma of the right temporal lobe diagnosed in 1992. The patient died 30 June 2003 due to aspiration pneumonia associated with a persistent vegetative state, which resulted from gradual tumor progression. Patient failed prior chemotherapy, surgery, and radiation, and was begun on Poly ICLC in 1993 on a compassionate basis on this protocol. Patient was already in a vegetative state at start of Poly ICLC. There was no hematologic or other toxicity present to this medication. Per telephonic discussion with initial PI, all glioma patients are off Poly ICLC for several years, with four of the initial thirteen patients treated with Poly-ICLC still doing well 8-12 years later. Per telephonic discussion with PI of a phase II study of Poly-ICLC in children with children with recurrent malignant and low-grade gliomas treated at Children's National Medical Center in Washington DC, one patient with malignant glioma completed Poly-ICLC three years ago and is "doing well", and two other children with grade II (low-grade) glioma are also two years off therapy and "doing well". Results are not published, and additional details are not available to PI.

### CONCLUSIONS

All MS patients have transitioned to one of the FDA approved Multiple Sclerosis medications. One glioma patient who was on Poly-ICLC on a compassionate use basis died 30 June 2003.



## DETAIL SUMMARY SHEET

TITLE: Markers of Possible Vulnerability to Symptoms Following Traumatic Brain Injury

KEYWORDS: traumatic brain injury, moderate head injury

PRINCIPAL INVESTIGATOR: Deborah L. Warden, MD

DEPARTMENTS: Neurology

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 04 August 1998

### STUDY OBJECTIVE

To explore possible relationships between biologic factors, i.e., certain allelic frequencies, and response to injury following TBI.

### TECHNICAL APPROACH

Genotyping banked blood samples to identify ApoE and serotonin transporter genotypes. Other allelic frequencies may be analyzed subsequently. The blood samples used in this protocol will be obtained from WU #7144 and WU #7154. These are protocols on traumatic brain injury. (TBI.) In both cases, patients gave informed consent for the use of their blood in experimental tests. A "firewall" has been constructed to protect the confidentiality of each participant. This protocol was initiated because these blood samples from Work Units 7144 and 7154 represent an opportunity to begin to understand possible relationships between polymorphisms and recovery from head injury. Patients were geographically dispersed, and in one case, a patient had died from unrelated causes since enrolling in the protocol. It was unlikely that these patients could be re-contacted for a separate consent, and a new sample could take several more years to obtain. The specific plan is as follows: Genetic Polymorphism Determination: Each case subject is characterized with respect to known polymorphism related to brain function and/or TBI. Methods include using a polymerase chain reaction (PCR)-based approach based on the published primer sequences. We obtain data on the frequency of functional and non-functional polymorphisms for each gene to be analyzed. Allele frequencies for the experimental population are determined and compared with known gene frequencies in the general population. Data are statistically analyzed for significant correlation with results obtained from neuropsychological testing, neuropsychiatric evaluation, and other clinical indices. The sample size includes 239 specimens from Work Units 7144 and 7154. Association of behavioral phenotype with a specific genotype will be determined by calculating odds ratios (OR) and confidence intervals using multivariate logistic regression models. Data will be adjusted for confounding factors such as changing allele frequency with age and sex. A two-sided p value will be used for all statistical tests.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Over the past year, collaboration has continued with Dr. Lipsky to explore the effects of genetic markers - specifically those effecting neurotransmitter effects - on patterns of TBI recovery. Analyses have been performed to examine the role of the COMT polymorphism in cognitive recovery after TBI. Results of these analyses were presented at the Annual Meeting of the American Neuropsychiatric Association (ANPA) meeting in La Jolla, CA in February of 2002. A manuscript describing these results has been submitted for publication to Biological Psychiatry. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 239.

### CONCLUSIONS

Analyses of COMT polymorphism effects on executive functioning following TBI have yielded interesting results that have been presented and have been submitted for full publication. Future analyses will examine the relationship of other genetic polymorphisms to TBI recovery.

## DETAIL SUMMARY SHEET

TITLE: The Neuroprotective Effect of Non-NMDA Receptors in Cultured Rat Cerebellar Granule Cells From Sprague-Dawley Rats Pups

KEYWORDS: AMPA, trans-ACPD, kainic acid, aniracetam, neuroprotection, excitotoxicity

PRINCIPAL INVESTIGATOR: Marini, Ann MD

ASSOCIATES: Krishna Banaudha, Ph.D

DEPARTMENT: Neurology

STATUS: C

SERVICE:

INITIAL APPROVAL DATE: 17 November 1998

### STUDY OBJECTIVE

To determine whether non-N-methyl-D-aspartate receptors protect neurons against the excitotoxic effects of glutamate acting on N-methyl-D-aspartate receptors.

### TECHNICAL APPROACH

We are using cultured rat cerebellar granule cells to achieve our objective outlined above. These neurons are relatively homogeneous and express all of the glutamate receptor subtypes including N-methyl-D-aspartate and non-N-methyl-D-aspartate receptors. Cerebellar granule cells are pretreated with variable concentrations of specific non-N-methyl-D-aspartate receptor agonists followed by treatment with an excitotoxic concentration of glutamate (100  $\mu$ M). Twenty-four hours later the number of viable cells are quantified using fluorescein diacetate.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Never received sufficient funding to carry out project.

### CONCLUSIONS

No progress.

## DETAIL SUMMARY SHEET

TITLE: The Frequency and Nature of Forensic Issues in an Inpatient Adult General Psychiatric Population.

KEYWORDS: Forensic psychiatry, Military psychiatry

PRINCIPAL INVESTIGATOR: Grieger, Thomas A., CAPT MC USN  
ASSOCIATES:

DEPARTMENT: Psychiatry  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 25 March 1998

### STUDY OBJECTIVE

This study will tabulate the frequency and nature of forensic issues in adult psychiatric inpatients admitted to this facility and examine for relationships between these issues and demographic and clinical variables.

### TECHNICAL APPROACH

Retrospective chart review.

### PRIOR AND CURRENT PROGRESS

Chart review and data entry complete, data analysis in process. No adverse events, no presentations, no publications, or new literature that would change the nature of the study or its relevance.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 301. The total number enrolled study-wide is 301, if multi-site study.

### CONCLUSIONS

None to date.

## DETAIL SUMMARY SHEET

**TITLE:** Comparison of Parental Therapeutic Alliances Before and After Initial Psychiatric Interviews: Telepsychiatry Versus In-Person Appointments

**KEYWORDS:** Therapeutic Alliance, Telepsychiatry

**PRINCIPAL INVESTIGATOR:** MAJ Nancy Black, MD

**ASSOCIATES:** LTC Stephen Cozza, MD; Ms. Sarah Rosquist

**DEPARTMENT:** Psychiatry

**STATUS:** O

**SERVICE:** Child and Adolescent Psychiatry

**INITIAL APPROVAL DATE:** 17 November 1998

### STUDY OBJECTIVE

The objectives of this study are to examine the elements of the developing therapeutic alliance from the first psychiatric interview based upon the parental perspective. The primary distinction will be made in determining whether there is a significant difference between the questionnaires obtained from in-person interviews and those obtained from telepsychiatry interviews. Another objective is to compare the parental opinions both before and after interviews.

### TECHNICAL APPROACH

Questionnaires approved by WRAMC human use committee will be distributed to all participants who consent in both in-person and telepsychiatry initial intakes done by staff at the Child and Adolescent outpatient clinic at WRAMC. These questionnaires are designed to quantify parents' perceptions of the potential for an alliance to be made between the provider and the patient/family. All participants will also fill out the YOUTH OUTCOME QUESTIONNAIRE (YOQ™2.0 (1) which is already part of the paperwork involved with an initial intake. Symptom Severity Data obtained from the YOUTH OUTCOME QUESTIONNAIRE (YOQ™2.0 (1) will be used to match the in-person and telepsychiatry participants by level of severity. These matched groups then will be examined to determine if any statistically significant trends regarding parental perception of the potential for alliance to form exist. A post interview questionnaire will be given to parents of the telepsychiatry group to monitor any change of their perceptions of the ability to form alliance before and after the interview. The number of complete, usable data sets is 40 telepsychiatry cases and the 100 in-person cases. Please see the attached addendum for proposed procedural changes.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There is no literature that looks specifically at satisfaction with child and adolescent telepsychiatry. Initial trends indicate that participants in the telepsychiatry group have higher expectations prior to their initial interview than do participants in the in-clinic group. Additionally, participants in the telepsychiatry group seem to be satisfied with the services they receive via telepsychiatry, based on the change in the mean scores from the pre-interview questionnaire to the post-interview questionnaire. (Scores decreased, and lower scores are associated with greater satisfaction.) No significance to date between research groups, but data collection is still on going. The number of subjects enrolled to the study since last APR at WRAMC is 48 and the total enrolled to date at WRAMC is 100. The total number enrolled study-wide is 131, if multi-site study.

### CONCLUSIONS

Data collection is ongoing at the distant site; data collection is complete at WRAMC. An attempt was made to recruit Fort Detrick, but was unsuccessful due to staffing/credentialing issues.

## DETAIL SUMMARY SHEET

**TITLE:** Assessing Pre-Military Psychiatric Illness, Risk Factors Leading to Early Onset of Psychiatric Illness and Inter-Rater Reliability of Psychiatric Diagnosis

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** Ritchie, E. Cameron LTC MC

**ASSOCIATES:** Grammer, Geoffrey G. CPT (P) MC, Cooper, Mark CPT MC, Grieger, Thomas CPT MC

**DEPARTMENT:** Psychiatry

**STATUS:** C

**SERVICE:**

**INITIAL APPROVAL DATE:** 02 February 1999

### STUDY OBJECTIVE

1. To determine if patients had active symptoms or prodromal signs of illness prior to entering the military.
2. To examine precipitating stressful life events for military personnel that were admitted to inpatient psychiatric wards at WRAMC.
3. To document the accuracy of DOD diagnoses.

### TECHNICAL APPROACH

No change, retrospective chart review.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The comparison between the diagnoses made by the WRAMC physicians in the medical record and the diagnoses from the independent blinded reviewers has been completed.

The original protocol asked for permission to review up to 400 charts. These were charts of patients who were hospitalized in the first year of active duty. However, fewer charts than expected had patients who were hospitalized within a year and whose charts contained enough information to analyze.

The data from 69 inpatient charts on prodromal signs of illness had been compiled and partially analyzed. However, there were some difficulties with the initial collection and analysis of the data, and it had to be re-done. The data has been entered into a new spreadsheet. Analysis is pending.

Because of time and resource limitations, it was decided not to attempt to analyze psychological testing or MRI data. There have been no new subjects enrolled. This is a retrospective chart review. Therefore there have been no adverse actions or patients withdrawn from the protocol. Paper is in final stages of review prior to submission.

### CONCLUSIONS

There is excellent diagnostic reliability between the WRAMC physicians and blinded reviewers. The kappa for inter-rater reliability was .84. This kappa is a chance-related reliability measure. The uncorrected percent agreement between the independent psychiatrists and the Medical Board was 88%. The main source of discrepancy came from questions about the length of illness, which occasionally was not well documented in the Medical Board.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 69.

## DETAIL SUMMARY SHEET

TITLE: Analysis of Component Neurocognitive Processes for the Trial-Making Test - An Examination of Age Related Changes

KEYWORDS: Trail Making Test, Aging

PRINCIPAL INVESTIGATOR: Jones, Alvin Ph.D., DAC

ASSOCIATES: Axelrod, Brenda M.A.

DEPARTMENT: Psychology

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 8 July 1997

### STUDY OBJECTIVE

There are three objectives:

- (1) To determine if the component neurocognitive process (motor speed, visual scanning etc.) can be determined and reliably measured for the Trial Making Test;
- (2) To examine the effects of age on the component neurocognitive processes;
- (3) Establish preliminary normative data for clinical interpretation of test results.

### TECHNICAL APPROACH

There are three phases of research:

- (1) Development of standardized test materials;
- (2) Establishing test-retest reliability for the testing material;
- (3) Collection of data to examine how performance changes on the component neurocognitive process over the life span. The final stage will also provide preliminary normative data for clinical interpretation of test results.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Data is in process of being analyzed; there are no current findings. No adverse events have occurred. No amendments have been made.

The number of subjects enrolled to the study since last APR at WRAMC is 102 and the total enrolled to date at WRAMC is 106.

### CONCLUSIONS

None.

## DETAIL SUMMARY SHEET

TITLE: Evaluation of Telesurgical/Robotic Presence

KEYWORDS: Telesurgical mentoring, urology, telestration, robotics

PRINCIPAL INVESTIGATOR: Schenkman, Noah LTC MC  
ASSOCIATES:

DEPARTMENT: Telemedicine  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 25 November 1997

### STUDY OBJECTIVE

The purpose of this study is to establish a telesurgical presence program between Walter Reed Army Medical Center, John Hopkins University and Ft Detrick, MD and evaluate the feasibility of telementoring less experienced surgeons, fellows, residents and medical students during open surgical cases and endoscopic surgery. Additionally, the use of a remotely controlled robotic arm to hold a laparoscope, as the laparoscopist's assistant, will be evaluated at these longer distances to determine the effect if any on remote telementoring. This system will in turn serve as the test bed for future telesurgical applications as they are: developed and as a remote site for future deployed telesurgical systems.

### TECHNICAL APPROACH

This proposal will evaluate the feasibility of telementoring both laparoscopic and open surgical procedures using telecommunications links between John Hopkins University, Ft. Detrick and Walter Reed Army Medical Center. We will use a T-1 PRI telecommunications link for Video Tele-Conferencing (VTC) and remote control of the AF-SOP robotic arm that holds the laparoscope. We will also employ a whiteboarding function to telestrate the procedures. Our goal is to establish that this sort of remote mentoring of surgical procedures is feasible and can be potentially applied to the far-forward military medical facilities in times of combat and also for medical education procedures.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

To date we have been unable to start the protocol due to the ongoing and delayed renovations of the WRAMC operating rooms, now entering their 3rd year. We anticipate resuming this protocol once these renovations are complete in early 2003.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS:

We are currently expecting to resume this protocol when practically feasible pending operating room availability.

## DETAIL SUMMARY SHEET

TITLE: Clinical Evaluation of a High-Resolution Digitized Stereo Video Slit Lamp for Use in Teleophthalmology

KEYWORDS: telemedicine, ophthalmology, diagnosis, digital images, slit lamp biomicroscopy, anterior segment

PRINCIPAL INVESTIGATOR: Bower, Kraig LTC MC

ASSOCIATES: CPT Erik Niemi, MC; COL (Ret) Kenyon Kramer; LTC Edward Trudo, MC

DEPARTMENT: Telemedicine

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 14 July 1998

### STUDY OBJECTIVE

The purpose of this study is to compare the clinical diagnostic performance of the high resolution digitized stereo video slit lamp with in-person slit lamp examination in patients presenting to a general ophthalmology clinic.

### TECHNICAL APPROACH

This is a prospective observational study. Investigators at Walter Reed Army Medical Center Ophthalmology Service and the John Moran Eye Center at the University of Utah will select consecutive patients from their clinics according to the previously published inclusion/exclusion criteria. A total of 50 patients will be recruited from each site. Each patient will be identified with a distinct ID number. The investigator will perform a standard clinical slit lamp exam on both eyes and note all findings in the patient chart and on the study exam report form. The patient will then be examined with the video digital slit lamp according to a standard protocol. The patients will resume the intended course of treatment for the remainder of their appointment. The video, digitized exams will be evaluated by masked reviewers at both institutions at a time subsequent to the actual patient exams. Using the live exams as the gold standard, the proportion of correct diagnosis made using the video exam will be described using proportions with 95% confidence intervals (CI).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are no new subjects enrolled at either site and we do not plan on enrolling any new subjects in the protocol as written. Dr. Subramanian is working on a modification that will allow subset analysis of corneal transplant subjects. He is currently away completing fellowship training, and will resume the modification on his return in August. If at that time he does not wish to pursue the modification we will close the protocol.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 29. The total number enrolled study-wide is 71, if multi-site study.

### CONCLUSIONS

The digital video slit lamp has moderate utility in the remote diagnosis of anterior ocular findings. However, the exam is difficult and time consuming, and since the onset of this study, imaging technology has advanced a great deal. Nevertheless, the protocol has proven safe and reasonably effective for some forms of eye disease. Further investigation may be warranted.



## DETAIL SUMMARY SHEET

TITLE: Molecular Epidemiology of HIV-1 in Military Populations.

KEYWORDS: HIV, military, seroconvertors

PRINCIPAL INVESTIGATOR: Aronson, Naomi COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Infectious Disease

STATUS: C  
INITIAL APPROVAL DATE: 30 September 1997

### STUDY OBJECTIVE

To describe the subtype and viral resistance patterns of HIV seroconverting military personnel correlating this with information regarding deployment, risk behaviors, potential contributing factors, in order to target military populations for intensive prevention training programs.

### TECHNICAL APPROACH

All military seroconvertors (in past four years) are eligible. Serum is obtained for genetic HIV subtype testing. Genotypic HIV viral resistance determinations are performed on all samples with detectable viral loads. The participant fills out a confidential survey instrument. Addendum to assess phenotypic resistance in a subpopulation. Addendum to allow banking of samples by patient identification number in the HIV repository. Addendum submitted currently to assess Kaposi Sarcoma Virus (KSV) and Herpes Simplex Virus Type II antibodies correlated with reported risk exposures. Subject enrollment will stop 31 July 2001 at all study sites.

### PRIOR AND CURRENT PROGRESS

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 86. The total number enrolled study-wide is 603. There are no adverse events reported and no withdrawals from the protocol at WRAMC. Information at other sites is not known. No direct benefit accrued to participants. A protocol deviation was submitted in November of 2001 due to funding withdrawal and end of support of database entry at NHRC. Two subjects were not given the follow-up six-month repeat questionnaire.

### CONCLUSIONS

About 4% of WRAMC HIV seroconvertors were non B HIV subtype and 14% that were HIV drug naïve had genotypic signs of resistance to at least one antiretroviral. Acquisition of non B HIV subtypes is associated with overseas deployment. HIV seroconversion was associated with high use of alcohol, poor condom compliance, and frequent casual sex partner exposure in the seroconverter window. Numerous areas for further intervention for prevention of HIV in active duty military have been identified.

## DETAIL SUMMARY SHEET

TITLE: A Tri-service Study of Human Immunodeficiency Virus Disease in United States Military Beneficiaries

KEYWORDS:

PRINCIPAL INVESTIGATOR: Hawkes, Clifton LTC MC

ASSOCIATES:

DEPARTMENT: Medicine

SERVICE: Infectious Disease

STATUS: O

INITIAL APPROVAL DATE: 31 March 1995

### STUDY OBJECTIVE

To systematically document the natural disease progression of HIV infection and the effect of therapeutic intervention on the course of the disease. To study factors related to HIV transmission in sexual partners not yet infected with HIV. To develop and evaluate new and/or improved laboratory methods for diagnosing and staging HIV disease.

### TECHNICAL APPROACH

Medical information related to HIV disease is routinely being collected as part of the standard of care for HIV patients. This information will be collected and organized into a computerized database, which will facilitate scientific review and assist in the generation of hypotheses, which can then be tested utilizing various statistical analyses. Blood that is collected will be used to identify new methods of detecting replicating HIV virus, as well as patterns and mechanisms of resistance. Safeguards to patient confidentiality are met. This database forms the core around which other specific protocols can be built.

### PRIOR AND CURRENT PROGRESS

The number of subjects enrolled to the study since last APR at WRAMC is 20 and the total enrolled to date at WRAMC is 461. The total number enrolled study-wide is 1762, if multi-site study. There have been two serious adverse events involving deaths of study participants. To date, no immediate cause of death has been identified for either patient.

### CONCLUSIONS

No final conclusions reached during this reporting period. Data collection continues.

## DETAIL SUMMARY SHEET

**TITLE:** A Phase I/II Study of the Safety, Survival, and Trafficking of Autologous CD4-zeta Gene-Modified T Cells with and without Exogenous IL-2 in HIV Infected Patients

**KEYWORDS:** HIV, gene therapy

**PRINCIPAL INVESTIGATOR:** Aronson, Naomi COL MC

**ASSOCIATES:** Wortmann, Glenn LTC MC; Bernstein, Wendy COL MC; Cash, Brooks LT MC; Mulhall, Brian MAJ MC; Gibbs, Barnett MAJ MC

**DEPARTMENT:** Medicine

**SERVICE:** Infectious Disease

**STATUS:** O

**INITIAL APPROVAL DATE:** 19 January 1999  
Six-Month Review

### STUDY OBJECTIVE

To assess the safety, tolerability, and feasibility of administering an infusion of autologous CD4 zeta gene modified CD4+ T cells in an outpatient setting of highly active antiretroviral therapy (HAART) with and without IL-2 at a maximum non-toxic daily dose of 1.2 M IU/m<sup>2</sup> subcutaneously daily for 56 days. Assess the effect of daily subcutaneous IL2 on the persistence and trafficking of CD4 zeta gene-modified T cells in the circulation and lymphoid (rectal) tissue. Determine the effect of CD4 zeta infusion with and without IL-2 on viral load (plasma HIV-1 RNA, tissue HIV-1 RNA, and frequency of latent replication competent HIV-1 in PMBCs).

### TECHNICAL APPROACH

This 3-arm, randomized study of gene modified costimulated T cells (about 10<sup>10</sup> infused) with or without daily subcutaneous IL-2 in HIV patients with undetectable viral load has an active interventional duration of 20 weeks. Replication competent retrovirus will be intermittently checked for as long as the individual agrees to participate. Rectal biopsy and peripheral blood mononuclear cells will be assessed for viral load and latent replication, as well as CD4 zeta. Assays to include cytotoxic lymphocytes, neutralizing antibody and lymphocyte proliferation assays are planned to assess the helper effect of CD4 zeta T cell infusion. A questionnaire to assess long-term understanding of protocol was added after intervention completed. An addendum added another sampling of rectal tissue and PBMC at one year (visit QF4A) past the end of intervention period. This is to assess persistence of the zeta vector and host immune function.

No new literature findings that are directly relevant to this study. News release of leukemia diagnosed in a SCID child who received a different stem cell gene therapy, but with the same retroviral vector as contained in our study. This event is thought by the investigator to represent potential insertional mutagenesis. This risk is discussed in our consent form as well as introductory briefing.

In our study, interventions to date have been well tolerated. There have been two serious adverse events, both occurring during the screening period (before any intervention received), of grade 4 toxicity of liver function tests (attributed to acute hepatitis C) and a hospitalization for cardiac evaluation finding severe peripheral and cardiovascular atherosclerosis which was requiring bypass and endarterectomy. Both patients were terminated from the study prior to intervention. Since the last annual report, we have added one addendum that extended the immune function assays and zeta gene persistence studies to one year beyond the end of the intervention period. The number of subjects enrolled to the study since last APR at WRAMC is 3 and the total enrolled to date at WRAMC is 13.

### CONCLUSIONS

To date, the IL-2 and CD4 zeta gene modified T cell infusions seem well tolerated by the twelve subjects who have entered the interventional phase of the protocol.

## DETAIL SUMMARY SHEET

**TITLE:** A Phase I/II Study of the Safety, Survival, and Trafficking of Autologous CD4-zeta Gene-Modified T Cells with and without Exogenous IL-2 in HIV Infected Patients

**KEYWORDS:** HIV, gene therapy

**PRINCIPAL INVESTIGATOR:** Aronson, Naomi COL MC

**ASSOCIATES:** Wortmann, Glenn LTC MC; Bernstein, Wendy COL MC; Gibbs, Barnett MAJ MC, Mulhall, Brian MAJ MC, Happe, Mark CPT MC

**DEPARTMENT:** Medicine

**SERVICE:** Infectious Disease

**STATUS:** O

**INITIAL APPROVAL DATE:** 19 January 1999

Six-Month Review

### STUDY OBJECTIVE

To assess the safety, tolerability, and feasibility of administering an infusion of autologous CD4 zeta gene modified CD4+ T cells in an outpatient setting of highly active antiretroviral therapy (HAART) with and without IL-2 at a maximum non-toxic daily dose of 1.2 M IU/m<sup>2</sup> subcutaneously daily for 56 days. Assess the effect of daily subcutaneous IL2 on the persistence and trafficking of CD4 zeta gene-modified T cells in the circulation and lymphoid (rectal) tissue. Determine the effect of CD4 zeta infusion with and without IL-2 on viral load (plasma HIV-1 RNA, tissue HIV-1 RNA, and frequency of latent replication competent HIV-1 in PMBCs).

### TECHNICAL APPROACH

This 3-arm, randomized study of gene modified costimulated T cells (about 10<sup>10</sup> infused) with or without daily subcutaneous IL-2 in HIV patients with undetectable viral load has an active interventional duration of 20 weeks. Replication competent retrovirus will be intermittently checked for as long as the individual agrees to participate. Rectal biopsy and peripheral blood mononuclear cells will be assessed for viral load and latent replication, as well as CD4 zeta. Assays to include cytotoxic lymphocytes, neutralizing antibody and lymphocyte proliferation assays are planned to assess the helper effect of CD4 zeta T cell infusion.

### PRIOR AND CURRENT PROGRESS AND REVIEW OF RECENT LITERATURE

No new literature findings that are directly relevant to this study. Two cases of leukemia diagnosed in SCID children who received a different stem cell gene therapy but with a similar retroviral vector as contained in our study led to a voluntary halt in enrollment. Both SCID gene therapy study events are found by the investigator to represent potential insertional mutagenesis in or near the LM02 site. The RAC held an emergency meeting and reviewed the events and it was felt that current evidence supported safety and lack of generalizability to this study of differentiated T cells. This risk is discussed in detail in our consent form as well as introductory briefing. We have added an amendment for additional safety including clonal analysis studies for fifteen year after infusion for early clonal expansions.

In our study, interventions to date have been well tolerated. Unexpected adverse events, adverse events, and serious adverse event have been reported to DCI. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 13.

### CONCLUSIONS

To date, the IL-2 and CD4 zeta gene modified T cell infusions seem well tolerated by the eleven participants who have entered the interventional phase of the protocol. We have begun to evaluate interim laboratory investigations, and find that CD4 zeta marked cells enter and survive in the circulation for the treatment period. In addition, high rates of apoptosis are reduced and levels of natural killer activity can be increased.

## DETAIL SUMMARY SHEET

TITLE: Antibiotic Treatment of Gulf War Veterans' Illnesses (CSP 475)

KEYWORDS: Gulf War Veterans' Illnesses, antibiotic, doxycycline, Mycoplasma, chronic fatigue, neurocognitive dysfunction, joint pain

PRINCIPAL INVESTIGATOR: Engel, Charles LTC MC

DEPARTMENT: Deployment Health Clinical Center  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 23 March 1999

### STUDY OBJECTIVE

The primary objective is to determine whether a 12-month course of doxycycline treatment in deployed Gulf War veterans presenting with Gulf War Veterans Illnesses and testing as mycoplasma positive improved patients' functional status. The secondary objectives are to determine whether doxycycline treatment reduces symptoms of Gulf War Veterans Illnesses, including pain, fatigue and neurocognitive concerns, whether doxycycline treatment converts mycoplasma (+) patients to mycoplasma (-) status. If so, it will be determined whether these subjects revert to mycoplasma (+) status when doxycycline treatment terminates. Also, the relationship of changes in mycoplasma status will be associated with changes in functioning and symptoms. Finally, we will determine if the benefits of 12 months doxycycline treatment persist after termination of treatment.

### TECHNICAL APPROACH

The study employs a randomized, double blind design that compares two groups of patients. All veterans who were on active duty, or in the National Guard, or the Reserves between August 1990 and August 1991 and were deployed to Gulf region during that time are considered for participation. To be eligible, a veteran must have at least two of the following three symptoms that began after August 1990, have lasted for more than six months and are occurring up to the present:

- a) Fatigue that limits usual activities (work, recreation, or social)
- b) Musculoskeletal pain involving two or more regions of the body, and
- c) Neurocognitive dysfunction (self-reported difficulties in memory, concentration or attention) and
- d) Must test as mycoplasma positive on PCR testing by central laboratory.

Patients meeting all enrollment criteria and who give informed consent to participate in the study are randomized to one of the following two groups. In the first group, the patients will be treated with doxycycline for 12 months and the second group will be treated with placebo for 12 months. Patients who are assigned doxycycline receive 200mg/day. They are instructed to take their pill the same time each day, preferably in the morning. Patients assigned to the placebo group receive identical appearing medication preparations. Because doxycycline can cause photosensitivity to sunlight, all patients are provided with a potent sun block preparation. All patients receive the study drugs for one year. Patients are followed for an additional six months after cessation of study drugs to determine relapse rates. Major patient assessments are completed at baseline and at 3,6,9,12 and 18 months. Major assessment consists of the SF-36V, the McGill Pain Questionnaires, the Multidimensional Fatigue Inventory, the Cognitive Failures Questionnaire and the Gulf War Illness Questionnaire. Monthly follow-up visits are done to dispense medication, check compliance, and obtain data on hospitalizations and clinic visits. The use of PCR for detection and identification of *Mycoplasma* species is done at 0, 6, 12 and 18 months.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 13. The total number enrolled study-wide is 491, if multi-site study.

Work Unit # 8900-99 [*Continued*]

Of the 13 subjects who were enrolled, 3 were lost to follow-up and the remaining 10 completed the study. The last patient was seen on October 15, 2001.

Despite the fact that this study was completed during the fall of 2001, the project remains ongoing pending the release of study results to the participating patients. This disclosure of study findings will be concurrent with the publication of a manuscript that has been prepared but is not yet in press. Therefore, there have been no new findings, amendments or modifications of the protocol since the last review. In addition, no adverse events, either locally or with respect to the other 27 participating sites, have been observed. Analysis of the study data has revealed no statistically significant difference between the placebo group and treatment group with respect to the primary outcome measure (i.e. an improvement of greater than 7 units of the SF-36V score at 12 months of treatments relative to baseline).

CONCLUSIONS

There is no statistically significant difference between the placebo group and treatment group with respect to the primary outcome measure (i.e. an improvement of greater than 7 units of the SF-36V score at 12 months of treatments relative to baseline).

## DETAIL SUMMARY SHEET

TITLE: A Randomized, Multicenter Controlled Trial of Multi-Modal Therapy in Veterans with Gulf War Illnesses (CSP 470)

KEYWORDS: aerobic exercise, Gulf War Veterans Illness, cognitive behavioral therapy, fatigue, memory loss, joint pain

PRINCIPAL INVESTIGATOR: LTC Charles C. Engel, MC

DEPARTMENT: Deployment Health Clinical Center  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 23 March 1999

### STUDY OBJECTIVE

#### Primary Hypothesis

The primary hypothesis of this study is that both aerobic exercise and cognitive behavioral therapy will significantly improve physical function (as measured by the Physical Component Scale of the SF-36V) in veterans with Gulf War Illness (GWI), and the combination of cognitive behavioral therapy and aerobic exercise will be more beneficial than either therapy alone.

#### Secondary Hypothesis

1. Both aerobic exercise and CBT will lead to improvements in the cardinal symptoms of GWI.
2. Both aerobic exercise and CBT will lead to decreased levels of distress in persons with GWI.
3. Both aerobic exercise and CBT will lead to improvements in emotional functioning in persons with GWI.

#### Tertiary Objectives

1. To determine which "process measures" play a role in achieving the desired outcomes. We will assess which of these mechanisms correlate with changes in each of the primary and secondary outcome variables, i.e. which process measures are mediators of outcome.
2. To develop a focus group consent document and compare its utility with the original study consent document with respect to patient-centered outcomes (recall, expectation of participation, availability of study personnel) and adherence to assigned therapy.
3. To develop a minimally clinically important difference for the Physical Component Scale of the SF-36V.

### TECHNICAL APPROACH

This clinical trial will study Gulf War era veterans who have unexplained chronic physical symptoms such as pain, fatigue, and/or cognitive difficulties. Patients will be randomized to one of four groups: 1) CBT plus aerobic exercise, 2) aerobic exercise alone, 3) CBT alone, and 4) usual and customary care. The primary outcome will be a clinically meaningful improvement in the Physical Component Summary scale of the SF-36V at one year relative to baseline. All patients will be followed over for one year and outcomes will be measured at 3 months, 6 months and 12 months post randomization.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no changes or new information since the last APR. There have been no new subjects enrolled and all subjects have completed all treatments. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 63. The total number enrolled study-wide is 1092, if multi-site study.

### CONCLUSIONS

Data analysis is still in progress, and as such, no conclusions have yet been made.

## DETAIL SUMMARY SHEET

TITLE: Are Heat Shock Proteins Target Antigens of the Immune System in Renal Allograft Recipients?

KEYWORDS: heat shock protein, kidney transplantation, immunology

PRINCIPAL INVESTIGATOR: LTC Christina Yuan MC

ASSOCIATES: John Swanson, Shirley Polly, Erin Bohen, Joyce Hershey

DEPARTMENT: Clinical Investigation

STATUS: C

SERVICE:

INITIAL APPROVAL DATE: 9 April 1996

### STUDY OBJECTIVE

1. To determine retrospectively and prospectively whether heat shock proteins (hsps) are target antigens of the immune system in renal allograft recipients. More specifically to determine if renal allograft recipients develop antibodies and/or cellular immune response specific for hsps.
2. To correlate development of humoral and/or cell-mediated immune responses specific for hsps with renal allograft outcome.

### TECHNICAL APPROACH

Phase I: This phase of the study is a retrospective cohort study. Fifty patients who have previously received a renal transplant and fifty age, sex and race matched controls will be selected for testing for anti-hsps antibodies (by ELISA), and for circulating T cells reactive to hsps (by flow cytometry).

Phase II: This phase of the study is a prospective cohort study. Forty consecutive subjects undergoing first cadaveric renal transplantation will be tested for anti-hsps antibodies and for T cells reactive to hsps immediately pre-transplantation and at serial time points post transplantation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

All patients and controls have been entered into this phase of the study—50 of each, for a total of 100 subjects. ELISA assays are completed. Results show that Hsp70 antibody levels are relatively less in patients vs. controls, as are Hsp27 antibody levels. Anti Hsp60 antibody levels were not statistically different between the two groups. Chart review is completed, as is data entry regarding donor-recipient matching. Phase II will not be undertaken. Closed to accrual; study is complete.

Some recent literature suggests that expression of 60 kd heat shock protein may precede rejection (Birk, et al, Proc Natl Acad Sci USA. 1999 96:5159); but there are no reports of antibodies against heat shock proteins being elevated in chronic rejections. A recent review points out that the role of heat shock proteins in allograft rejection remains undefined, although there are multiple reports of expression of various heat shock proteins during acute and chronic rejection (Pockley AG, Transplantation 2001 71:1503.) There have been no adverse events.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 100 (Phase I).

### CONCLUSIONS:

See above.



## DETAIL SUMMARY SHEET

**CURRENT TITLE:** Combination of Ribavirin with Interferon Alfacon-1 or with PEG Interferon Alfa 2b as Initial Treatment for Chronic Hepatitis C

**PREVIOUS TITLE:** (Prior to the addendum dated 2 January 2002) Combination of Ribavirin with Interferon Alfacon-1 or with Interferon Alfa 2b as Initial Treatment for Chronic Hepatitis C

**KEYWORDS:** hepatitis C, interferon, ribavirin, human trial

**PRINCIPAL INVESTIGATOR:** Maria Sjogren COL MC

**ASSOCIATES:** Kent Holtzmuller COL MC

**DEPARTMENT:** Clinical Investigation

**STATUS:** O

**SERVICE:**

**INITIAL APPROVAL DATE:** 15 December 1998

### STUDY OBJECTIVE

**NEW STUDY ARM** (addendum approved by HUC): To observe the response to interferon alfacon-1 in combination with ribavirin as compared to pegylated interferon alfa-2b and ribavirin in subjects with chronic hepatitis C infection.

**ORIGINAL STUDY ARM:** To observe the response to interferon alfacon-1 in combination with ribavirin as compared to interferon alfa-2b and ribavirin in subjects with chronic hepatitis C infection.

### TECHNICAL APPROACH

**NEW STUDY ARM** (approved by HUC): Subjects with established diagnosis of chronic hepatitis C (serology and liver biopsy) are randomized to one of two groups of therapy: interferon alfacon-1 and ribavirin or pegylated interferon alfa-2b and ribavirin. Subjects receive treatment for 24 weeks. At this point HCV RNA is tested in serum. If detectable, the subject does not continue therapy (both groups) - If HCVRNA is undetectable, treatment continues on for up to 48 weeks. Therapy is stopped at 48 weeks and subjects are monitored for an additional 24 weeks. A final test of HCV RNA is done at 72 weeks. If negative, the subject is a responder; if positive, the subject is a non-responder. A second liver biopsy will be done in patients who are responders.

**ORIGINAL STUDY ARM:** Subjects with established diagnosis of chronic hepatitis C (serology and liver biopsy) are randomized to one of two groups of therapy: interferon alfacon-1 and ribavirin or interferon alfa-2b and ribavirin. Subjects receive treatment for 24 weeks, at this point a HCV RNA is tested in serum. If detectable, the subject does not continue therapy (both groups). If HCVRNA is undetectable, treatment continues on for up to 48 weeks. Therapy is stopped at 48 weeks and subjects are monitored for an additional 24 weeks. A final test of HCV NA is done at 72 weeks. If negative, the subject is a responder; if positive, the subject is a non-responder. A second liver biopsy will be done in patients who are responders.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

**Recent literature** - Major studies have been published within the last 12 months suggesting that pegylated interferons may be more effective than standard interferons. The pegylated form is injected only once a week due to a prolonged and sustained half-life. Standard interferons are injected three times a week with an uneven level in serum. However, data from the original study arm of this protocol has shown that competitive efficacy of Interferon alfacon-1 compared to published data on pegylated interferons. Our study is a head to head comparison of consensus interferon plus ribavirin versus the only commercially available pegylated interferon.

Study Findings To Date - A total of 133 subjects were enrolled in the original arm of the study, 128 received therapy and 5 did not either because they removed consent or because of other personal factors. 77 were enrolled at Walter Reed and 56 at Kaiser Permanente. The treatment phase is completed for all 128 and 125 have completed the follow up observation period concluding their participation in the protocol. The last subject's observation will be completed in February 2003. To date, 55% of subjects randomized to Interferon Alfacon-1 and 39% of subjects randomized to Interferon Alfa 2b had undetectable levels of HCV at the end of the follow up period. The difference nears statistical significance ( $p = .054$ ) indicating that Interferon Alfacon-1 is more efficacious than Interferon Alfa 2b in our study. No study findings can be obtained thus far for the patients enrolled after the addendum; the majority of the patients are still on the study treatment.

Amendments and Modifications - Two addenda have been approved for this protocol since the time of the last annual progress report. The first addendum (2 January 2002) allowed no further patients to be randomized to the interferon Alfa 2b + ribavirin group based on research suggesting it was no longer the most efficacious form of treatment. Instead subjects were randomized to PEG interferon Alfa 2b + ribavirin. The other group remained the same. A quality of life questionnaire was added. An additional 100 subjects were allowed for enrollment. The data for the two arms of the study are being treated as separate. In the second addendum (18 March 2002) the dose of the study medication ribavirin was changed based on recent research findings. The dose was changed to reflect the patient's weight such that subjects weighing 75kg or less receive 1000 mg of ribavirin per day and subjects weighing more than 75kg receive 1200 mg of ribavirin per day. Previously all subjects received 800 mg ribavirin when combined with PEG-Interferon alfa 2b and 1000mg when combined with Interferon alfacon-1. Three depression inventories were also added to assess the severity and symptoms of depression in study patients. A memo (7 June 2002) was filed to request patient rollover from WU# 9221-99 to WU#02-92012. Subjects who were enrolled after the 2 January 2002 addendum to WU#9221-99 are on PEG Intron or Consensus Interferon. Those who are eligible for WU#02-92012 and still on treatment will be rolled over and the former study will be closed to enrollment. Conduct of the original protocol for WU#9221-99 will be closed when all patients have completed follow up (estimated February 2003). These patients were on Intron A or Consensus Interferon. They have all completed their course of treatment and will not be rolled over to WU#02-92012.

#### Number of Subjects Enrolled

ORIGINAL STUDY ARM: Since the last APR, no more patients were enrolled according to the original study arm (per 2 January 2002 addendum). However, in careful examination of the records, 1 patient had been left out from the database (VOL 005) by mistake - bringing the number of treated patients to 128, 77 at WRAMC. Another 5 patients were found to have been consented and randomized but never received therapy. These 6 patients have been added to the database because of the need to report data on all randomized patients per intention to treat.

NEW STUDY ARM (addendum approved by HUC): Since the last APR, the number of subjects enrolled in the new arm of the study at WRAMC and the total number at WRAMC is 22. The total number enrolled in the new arm study-wide is 38.

#### Withdrawals and Adverse Events

ORIGINAL STUDY ARM: 2 additional SAEs have been reported since the last APR. At WRAMC #33 discontinued due to anemia (Hgb 8.3). At Kaiser #247 discontinued due to sudden hearing loss. Reported in the last APR were 9 SAEs: At WRAMC hypothyroidism (x2 patients), variceal bleeding, persistent cough, skin rash, kidney stones, and psychiatric side effect. At Kaiser, palpitations & anemia (Hgb 9.0), gastrointestinal complaints.

#### Summary of expected AEs to date

Note that all symptoms are according to patient self-report. Baseline symptom report was subtracted from symptoms reported on treatment to obtain a more accurate measure of the drug side effects.

Flu-like (at least 2 of: fever, chills, myalgia, arthralgia): 89%	Nausea 66%	Hair Loss 61%
Fatigue 36%	Vomiting 29%	Injection Site reaction 49%
Headache 49%	Anorexia 69%	Concentration 62%
Cough 52%	Dyspepsia 53%	Insomnia 61%
Skin Rash 61%	Itching 67%	
	Depression 54%	
	Shortness of breath 69%	

Work Unit # 9221-99 [*Continued*]

NEW STUDY ARM (addendum approved by HUC): Since the last APR, 3 subjects were discontinued from treatment at week 24 as per protocol due to detectable HCV RNA. Two subjects were discontinued due to Serious AEs, both of which required hospitalization (#208 infection; #210 psychiatric event). Both SAEs were reported to HUC.

Summary of expected AEs to date

To date the expected AE experienced by patients are the common side effects as described in the consent form and similar to those reported for the original arm of the study (128 treated subjects).

CONCLUSIONS

The original arm of the study is almost completed and the new study arm is progressing well. Consensus interferon in combination with ribavirin appears to be promising therapy for chronic hepatitis C.

## DETAIL SUMMARY SHEET

TITLE: An Investigation of Oxidative Damage to Proteins in Thyroid Autoimmunity

KEYWORDS:

PRINCIPAL INVESTIGATOR: COL Henry B. Burch MC

ASSOCIATES:

DEPARTMENT: Clinical Investigation

STATUS: C

SERVICE:

INITIAL APPROVAL DATE: 6 April 1999

### STUDY OBJECTIVE

The objective of this protocol is to study the oxidative damage to proteins in thyroid autoimmunity. It has been established previously that compound Dityrosine is formed as a result of oxidation of proteins by free radicals. The free radicals are formed more in the disease condition than normal. Therefore, monitoring the level of Dityrosine is a useful tool to determine the oxidative stress in Autoimmune Thyroid disease. The protocol involves in the determination of the Dityrosine in the serum of Normal, Graves' and Hashimotos thyroiditis patients. The protocol proposes to assess the actual modification of the thyroid patients i.e. Thyroglobulin in the serum of patients with autoimmune thyroid disease by isolating and characterizing Tg in the serum.

### TECHNICAL APPROACH

Extraction and purification of Dityrosine from the serum was done by the following procedures:

- a. Digestion with Proteinase K to cleave Dityrosine from the proteins
- b. Separation and purification of the cleaved Dityrosine were done by centrifugation using Micron Centrifugal Filter devices.
- c. Eluate containing Dityrosine and other components of Mol.Wt. below 3,000 were treated with chloroform and 0.1% trifluoroacetic acid, centrifuged and aqueous layer collected and dried. The dried sample was dissolved in 0.1% TFA and injected to HPLC column. The chromatographic separation of the Dityrosine was achieved using Waters HPLC system, detected in Fluorescence detector. The mobile phase used for the separation of Dityrosine from the other components in the serum as following A) HPLC water with Pic B (1- Heptane Sulfonic Acid), B) 100% methanol with Pic B, C) 100% methanol, D) HPLC water. We used Waters Nova pack C 18 column and proper gradient profile.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is N/A and the total enrolled to date at WRAMC is N/A.

### CONCLUSIONS

No additional work will be done on this protocol. It is therefore closed.

## DETAIL SUMMARY SHEET

TITLE: Tacrolimus and Distal Renal Tubular Acidosis in the Rat.

KEYWORDS: tacrolimus, renal tubular acidosis, rats

PRINCIPAL INVESTIGATOR: CM Yuan, LTC MC

ASSOCIATES: Luana Kiandoli

DEPARTMENT: Medicine

SERVICE: Nephrology

STATUS: C

INITIAL APPROVAL DATE: 2 May 2000

### STUDY OBJECTIVE:

To develop a rat model of renal tubular (non-anion gap) acidosis due to tacrolimus administration. This syndrome is frequently observed in humans receiving the drug in immunosuppressive doses, but has not been described in rats.

### TECHNICAL APPROACH:

Forty-one rats (12 controls, 20 receiving 1 mg/kg/day tacrolimus (low dose), and 9 receiving 3 mg/kg/day tacrolimus (high dose) will be randomly entered. They will receive daily either tacrolimus PO in cherry syrup on a whole-wheat biscuit, or cherry syrup alone (controls) for up to 8 weeks. Tail blood will be drawn at 4, 6, and 8 weeks to determine presence of acidosis (defined as serum bicarbonate  $>3$  meq/liter lower than control animals), and tacrolimus level. Upon development of acidosis or at 8 weeks of treatment, animals will be placed in metabolic cages, and urine collected to determine urine anion gap and creatinine clearance. Animals will be anesthetized, aortic blood collected for blood gas determination, electrolytes, and BUN/creatinine. They will then be euthanized, and kidneys harvested for histopathologic evaluation. Up to two rats from each group will also undergo bicarbonate loading (per protocol) while anesthetized, to demonstrate the tubular site of acidosis.

### PRIOR AND CURRENT PROGRESS

Forty-one rats were treated with oral tacrolimus as per protocol, and all were euthanized in May/June 2002. There were no unexpected deaths; and all animals completed the experiment. Kidneys, serum, and plasma were collected as per protocol. Renal histopathology and serum chemistry is complete. The animals did not develop a significant metabolic acidosis at any time point. There was no significant histopathologic change - evidence that there was no permanent/irreversible renal damage due to the drug - which can occur at high doses. However, the rats did develop hypomagnesemia and excessive urinary magnesium excretion - which is seen in human patients treated with tacrolimus.

There have been no significant new findings in the literature that would impact on this study. No further animal work will be done. Closeout progress reports have been sent to AFIP IACUC. A paper is in preparation, and an abstract was submitted to this year's American Society of Nephrology Meeting.

### CONCLUSIONS

See above.

## DETAIL SUMMARY SHEET

TITLE: Measurement of Electrolytes in Microdialysis Samples by Mass Spectrometry

KEYWORDS: electrolytes, microdialysis, inductively-coupled plasma mass spectrometry

PRINCIPAL INVESTIGATOR: LTC James D. Oliver III, MC

ASSOCIATES: Yuan, Christina M., COL MC; Atkins, James L. COL MC; Abdel-Rahim, Maged M. MS; Morris, Elena R.; Pamnani, Motilal B. MBBS, Ph.D.

DEPARTMENT: Medicine

STATUS: O

SERVICE: Nephrology

INITIAL APPROVAL DATE: 01 August 2000

### STUDY OBJECTIVE

To measure potassium, calcium, and magnesium concentrations in microliter-volume samples obtained by the insertion of microdialysis probes in rat tissues (obtained under active animal use protocol USUHS #G176HX; administered and performed at USUHS). Please note: This protocol is not an animal research protocol, but a protocol for sample analysis. The samples come from an existing approved protocol at USUHS, Number APG-01-303.

### TECHNICAL APPROACH

This is an experimental laboratory protocol using existing samples obtained during the performance of an established USUHS animal use protocol (USUHS #G176HX). Twenty animals were approved for use in USUHS #G176HX. Interstitial electrolytes are measured using 15  $\mu$ l samples using inductively coupled plasma-mass spectrometry (ICP-MS) with internal standards as follows: Rb for K;  $^{44}\text{Ca}$  for Ca, and  $^{26}\text{Mg}$  for Mg.

### PRIOR AND CURRENT PROGRESS

Previously we validated the method for potassium/rubidium, and are performing routine measurements of K and Rb on the samples. We are still optimizing the analytical techniques for measuring isotopic ratios for Ca and Mg, attempting to minimize interferences from the Argon gas. We have looked into DRC technology as one means of doing this, and are considering the use of a high-efficiency nebulizing adapter as a complementary means.

### CONCLUSIONS

Interstitial potassium concentrations during hemorrhagic shock are elevated earlier, and to a greater degree, than intravascular concentrations. At this point, no clear trend has been seen in the calcium and magnesium concentrations.

## DETAIL SUMMARY SHEET

**TITLE:** ARBITER – Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol - A Randomized Trial Comparing the Effects of Atorvastatin and Pravastatin on Carotid Intima-Media Thickness

**KEYWORDS:** Randomized Trial, atherosclerosis, HMG-CoA reductase inhibitor

**PRINCIPAL INVESTIGATOR:** Allen J. Taylor LTC MC

**ASSOCIATES:** Louis Coyle DO, Patrick Flaherty DO, Thor Markwood MD, Steve Kent MD, Patrick G. O'Malley MD, MPH

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Cardiology

**INITIAL APPROVAL DATE:** 26 October 1999

### STUDY OBJECTIVE

To evaluate the relative effects of two different HMG-CoA reductase inhibitors on carotid atherosclerosis regression.

### TECHNICAL APPROACH

This study is a randomized study comparing the efficacy of atorvastatin and pravastatin on carotid atherosclerosis (carotid intima-media thickness). Patients beginning cholesterol lowering therapy who have a baseline serum cholesterol of 160mg/dL or greater and who are not currently on cholesterol lowering medication are randomized to one of 2 open-label treatment arms: pravastatin 40mg qd, or atorvastatin 80 mg qd. The primary endpoint is the change in carotid intima-media thickness over 12 months. Lab monitoring is performed at baseline, 3 and 12 months. The sample size for statistical significance is 132 patients. The protocol is approved for a maximum of 200 patients.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0, and the total enrolled to date at WRAMC is 161. Enrollment to new patients was closed in February 2001, and all patients have completed the one-year follow-up period. There were 20 study withdrawals, due to either patient request or drug intolerance. Thus, 141 patients, (with a required sample size of 132), completed the study. The study found that atorvastatin 80 mg/d lowered LDL cholesterol to a substantially greater degree than pravastatin 40 mg/d. This was associated with a greater degree of regression of atherosclerosis in the carotid artery (the primary endpoint of the study).

### CONCLUSIONS

The study has closed to enrollment and the principal results have been analyzed. Manuscripts are in press, and submitted as listed. Banked serum is still stored in locked secured freezer using anonymous identifiers. Future studies on these samples may be performed, after appropriate notification/review through DCI.

## DETAIL SUMMARY SHEET

TITLE: Galectin-3 Levels as a Marker of Thyroid Cancer in Fine-Needle Aspiration (FNA) Samples

KEYWORDS: Thyroid Cancer, FNA

PRINCIPAL INVESTIGATOR: LTC Victor Bernet, MC

ASSOCIATES: J. Anderson, Y. Vaishnav, B. Solomon, K. Burman, M. Ringel, M. Saji, C. Adair

DEPARTMENT: Medicine

STATUS: O

SERVICE: Endocrine

INITIAL APPROVAL DATE: 8 February 2000

### STUDY OBJECTIVE

- Confirm and expand the previously reported immunohistochemical findings that Galectin-3 staining is found predominantly in papillary and follicular thyroid cancer tissue in contradistinction to benign nodules and normal thyroid tissue.
- Develop a quantitative RT-PCR assay to measure levels of Galectin-3 in thyroid tissue.
- Assess the level of Galectin-3 mRNA expression in various types of benign and malignant thyroid histopathology samples.

### TECHNICAL APPROACH

Patients undergoing thyroidectomy for standard clinical indications consented to have their removed tissues be "snap frozen" in liquid nitrogen and stored at -70° C. In total, 38 such histopathologically diagnosed frozen tissue frozen tissue specimens consisted of 7 normal (NL), 9 benign (BN), 7 papillary thyroid cancer (PTC), 9 follicular thyroid cancer (FTC) and 6 follicular adenoma (FA) were included in this study. Genomic RNA from these frozen specimens was recovered using a standard Trizol method (Tri Reagent®, Molecular Research, Inc.) A quantitative RT-PCR was developed for Gal-3 using a sequence specific oligonucleotide probe and forward and reverse primers. A 103 bp long Gal-3 c-DNA segment, spanning the junction of exon 4 and 5 (GeneBank ACC# NM\_002306) was amplified using the forward primer: ACGGTGAAGCCCAATGCA and reverse primer TGACTCTCTCCTGTTGTTCTCATTGAA; and antisense probe AATGATGTTGCCTTCCACTTTAAC CCAGG labeled with 5'-reporter dye (FAM) and 3'-quencher dye (TAMRA). To help validate the kinetic quantitative RT-PCR method, human thyroid m-RNA (Clontech) was utilized for the construction of standard curves and GADPH (glyceraldehydes-3-phosphate dehydrogenase) m-RNA was used as an endogenous reference for Gal-3. The m-RNA templates were excluded from the negative standards. For each sample, the amount of target (Gal-3) and the endogenous reference were determined from the calibration curves. The target amount was then divided by the reference amount to obtain normalized values. Two techniques, agarose gel electrophoresis and cycle sequencing were utilized to confirm the identity of the PCR amplified 103 bp-c-DNA segment (Gal-3).

### PRIOR AND CURRENT PROGRESS

We have continued work on the use of Galectin-3 in FNA samples. Previous results found that RNA can indeed be isolated from diff-quick stained FNA slides, and we have identified the apparent best collection method and RT-PCR techniques for measurement of Gal-3 mRNA by quantitative RT-PCR. Also, we have been able to measure Galectin-3 mRNA levels in cytology from follicular adenomas and papillary thyroid cancer. We are presently involved in the last phase of this study and are collecting the final 180 prospective FNA samples of the initial 200 that were approved. We hope to show that Gal-3 mRNA collected from FNA samples can be used to distinguish benign from cancerous lesions. We expect to finish collection of these specimens sometime in the Spring 2003.

Recently published studies from other groups indicate that Gal-3 may indeed be a useful monitor marker for thyroid cancer. However, data still lacks on the usefulness of Gal-3 mRNA from FNA samples as



measured by QRT-PCR since most of the other studies deal with immunohistochemical analysis for Gal-3 expression. To date we have studied:

- 37 frozen specimens out of an approved number of 40
- 30 of 30 diff-quick FNA slides from pathology archives
- 10 of 30 samples from pathology archives approved in the addendum July 2001
- 105 of approved 200 samples prospectively collected as of 18 December 2002

The number of subjects enrolled to the study since last APR at WRAMC is 85. The total enrolled to date at WRAMC is 105.

#### CONCLUSIONS

- Results indicate that Gal-3 can indeed be amplified and quantitatively measured by RT-PCR from mRNA isolated from thyroid histology samples.
- Galectin-3 mRNA can be isolated from FNA samples either using diff-quick prepared slides or by washing the FNA needle hub at the time of the procedure. Use of diff-quick slides has the advantage of allowing the investigation to assess the cellularity present on the slide.
- Galectin-3 mRNA can be measured in benign and malignant cytology specimens.
- B-Actin or PBGD can be used as housekeeping products for assessment of Galectin-3 in FNA samples.
- Galectin-3 mRNA appears to be useful for distinguishing papillary thyroid cancer from benign samples. However, its usefulness for follicular thyroid cancer may be limited.
- The final phase of our study should help define if measurement of mRNA Gal-3 from FNA samples is an accurate and practical molecular marker for diagnosis of thyroid cancer.

## DETAIL SUMMARY SHEET

**TITLE:** The Effect of Helicobacter pylori Eradication on the Severity of Gastro-esophageal Acid Reflux as Determined by 24 Hours pH Measurement

**KEYWORDS:** H. pylori, Gastroesophageal Reflux

**PRINCIPAL INVESTIGATOR:** MAJ Brian P. Mulhall MC

**ASSOCIATES:** Roy Wong COL MC, Corinne Maydonovitch, Allan Andrews CPT MC, Roger Fincher MAJ MC

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Gastroenterology

**INITIAL APPROVAL DATE:** 18 January 2000

### STUDY OBJECTIVE

To assess the effect of H. pylori eradication on gastro-esophageal reflux and whether the pattern of the gastritis from H. pylori infection plays any role in potential changes in gastric acidity and associated gastro-esophageal reflux.

### TECHNICAL APPROACH

We plan to enroll 250 patients, with a goal of 80 patients completing the study (after several exclusionary steps). All adult patients presenting with gastro-esophageal reflux disease (GERD) symptoms will be offered participation. Serology for H. pylori IgG antibody will be performed to screen for H. pylori infection. Seropositive patients will undergo C-urea breath testing (UBT), to document active H. pylori infection and 24-hr esophageal pH testing and manometry to establish the presence and severity of GERD. A symptom questionnaire will also be completed. Patients with active H. pylori infection will undergo upper endoscopy and gastric biopsies. Histology will be used to determine the presence and pattern of gastritis and H. pylori. Four biopsies will be frozen for subsequent PCR analysis of the H. pylori genome to assess for virulence factors. Cag-A serology will be attained to assess its prevalence and relation to GERD severity. Patients will receive antibiotic therapy to eradicate H. pylori infection, and UBT will be repeated ten weeks later to confirm eradication. Patients then will have repeat 24-hr esophageal pH testing and symptom questionnaire to determine post-eradication GERD severity compared to pre-eradication status. The presence of antibodies to Cag-A will be compared to histological gastritis, GERD severity, and to post-eradication symptom changes. This study will provide a better understanding of the role of H. pylori and its eradication in GERD, and may have important implications in the management of GERD and H. pylori infections.

Protocol Addendum added Urea breathing testing to the initial evaluation in order to approximately document active H. pylori infection prior to endoscopy. This served to reduce up-front risk to the study patients who might eventually not be offered enrollment (due to H. pylori negativity). This has served to decrease institutional burden as well.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 7 and the total enrolled to date at WRAMC is 28 of 78 consented. (The total number consented study-wide is 79, with 29 that were H. pylori positive and 17 who have completed the study.)

Study enrollment was not actively pursued for the six months after the departure of Dr. Roger Fincher as efforts were being made (by Dr. Fincher) to concomitantly enroll patients at his new duty center. This protocol has been approved by EAMC DCI, but enrollment has been slow. The four patients enrolled prior to Dr. Fincher's departure successfully completed their pH and endoscopy studies this summer and Fall 2001 and all data have been collected and recorded. Another 38 patients have been interviewed for the protocol, but only 12 met

criteria and only 7 subjects were interested in enrollment. *H. pylori* culture has been completed and all data is logged into our data-base at present. As summarized in the listed abstracts, several conclusions been made from our preliminary data. Of the eight subjects that had completed the protocol in April 2001, 7/8 had successful eradication of their *Helicobacter pylori* with standard antibiotic therapy. Despite eradication of this organism, patient's overall Johnson/Demeester score (a measure of the degree of acid reflux) did not change substantially (from 27.0% to 26.9%). Symptom scores were likewise unchanged. This runs contrary to previous data arguing that eradication of *H. pylori* may actually increase GERD and GERD symptoms. We are planning another interim analysis when we reach 30 patients in the protocol, which should be in the next few weeks to months.

Seventeen patients enrolled up to April 2001 were demonstrated to have carditis (inflammation of the cardia of the stomach). Interestingly, the presence or severity of carditis did not correlate with the presence and severity of esophagitis 5 cm above the lower esophageal sphincter—though the severity of carditis did strongly correlate with the degree of antritis (antral inflammation). As such, this may argue that carditis is related more so to *H. pylori* infection than it is to GERD. Findings (regarding a specific type of cardia inflammation specifically correlated with *Helicobacter pylori*) conflicts with several recent studies, but replicates findings of el-Zimaity, Morini and Voutilainen. The latter study described carditis in patients without associated gastritis but correlated these findings with GERD-related esophagitis. Similarly, Bowrey also found carditis in distinct populations of patients with GERD or *H. pylori* and determined that the histological findings could only be distinguished with special stains. They propose that the carditis develops due to a similar immunological mechanism in both processes. Several studies have attempted to further delineate the relationship between *H. pylori* infection and GERD, but have been flawed because of retrospective design or small numbers of enrolled patients. Oberg completed a retrospective analysis on 229 patients with GERD or dyspepsia and found no relationship between complaints of GERD and *H. pylori* infection. They did not study organism eradication and its effects on GERD symptomatology. There is a great deal of ongoing interest in the relationship between *H. pylori* and GERD and the concomitant relationship that *H. pylori* and carditis. The studies cited and various expert opinion/reviews have not been yet produced resolutions on either issue.

The number of subjects enrolled to the study since last APR at WRAMC is 7 and the total enrolled to date at WRAMC is 29. The total number enrolled study-wide is 8, if multi-site study.

#### CONCLUSIONS

Preliminary data has been promising and the respective abstracts were met with interest at our professional meeting. Given the ongoing controversy, further investigation is warranted, and this study may be an important contribution to this continued quandary. Enrollment has slowed but will continue at WRAMC throughout 2002-2003 with a goal of completing enrollment in the spring of 2003, if intermediate analysis suggests adequate results.

## DETAIL SUMMARY SHEET

TITLE: A Comparison of Pediatric and Adult Colonoscopes in Adult Patients Presenting for Routine Colonoscopy

PRINCIPAL INVESTIGATOR: Cumings, Mark D. MAJ MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Gastroenterology

STATUS: C  
INITIAL APPROVAL DATE: 21 March 2000

### STUDY OBJECTIVE

To evaluate use of a pediatric colonoscope with an adult colonoscope by comparing a) total procedure time, b) time to reach cecum, and c) rate at which the endoscopist reaches the cecum.

### TECHNICAL APPROACH

Adult patients presenting to our clinic for colonoscopy will be assessed for entry in the study by the primary investigator prior to the date of the colonoscopy. The primary investigator, gastroenterology fellows, and staff will recruit patients at the time of initial patient interview with the physician. Prior to the initiation of the study, a randomization schedule will be used to assign subjects to either the pediatric or adult colonoscopy study groups. The primary investigator will contact patients prior to their scheduled colonoscopy to inquire about study participation. Those patients wishing to participate will then be evaluated for exclusion criteria. On the day of the procedure the patient will be consented by either the endoscopist or primary investigator. The GI staff will be aware of the assigned scope, but the patient will not know which scope is assigned. A gastroenterology staff physician will perform all endoscopies. Patients will undergo standard bowel preparation using Go-Lytely. All patients will receive the standard pre-procedure care: brief history by the nurse, insertion of a peripheral IV, recording of demographic data, and recording of initial vital signs. Pre-menopausal women will be required to undergo pregnancy testing with a qualitative urine pregnancy test prior to colonoscopy. During the procedure vital signs will be monitored every 5 minutes and recorded every 15 minutes. Patients will be provided sedation (opioids and benzodiazepines) prior to and during the procedure as deemed necessary by the endoscopist. The amount of time for each procedure will be recorded. Procedure start time will be the time the colonoscope is inserted into the anal canal. Procedure end time will be when the scope is removed from the patient. Time will be recorded in minutes and seconds. Both the total time it takes to reach the cecum (TTC) and total time for procedure (TTP) will be recorded. TTC is the length of time from insertion to visualization of cecal landmarks, to include ileocecal valve. TTP is the length of time from insertion to removal of scope from the patient. Prior to the start of the study, baseline times will be established for each staff by taking the average times of 10 procedures each using the pediatric scope and adult scope. Following the procedure the patient will be recovered for approximately one hour in the GI recovery area. Once recovered and prior to departing the clinic, the Endoscopic nurse will obtain pain and satisfaction scores from the patient using a visual analogue scale. The pain and satisfaction assessment will be repeated approximately 24 hours after the procedure.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No patients have been enrolled in this study. This study is closed because of no progress and because the PI has been transferred to Madigan AMC. The number of subjects enrolled to the study since last APR at WRAMC 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

Not applicable.

## DETAIL SUMMARY SHEET

**TITLE:** Tele-Hepatitis Phase I Validation of Desktop Video Teleconferencing (VTC) System at 384 kb ISDN for Evaluation of Patients with Hepatitis.

**KEYWORDS:** Telemedicine, VTC, hepatitis, ISDN

**PRINCIPAL INVESTIGATOR:** Inku Hwang

**ASSOCIATES:** Kent C. Holtzmuller, Michael A. Dunn, Maria H. Sjogren, Roy H. Wong, Ronald K. Poropatich

**DEPARTMENT:** Medicine

**SERVICE:** Gastroenterology

**STATUS:** O

**INITIAL APPROVAL DATE:** 16 May 2000

### STUDY OBJECTIVE

1. Determine the diagnostic concordance of visual physical exam findings in patients with chronic hepatitis using in person vs. desktop VTC at 128kb connection.
2. Determine the patient satisfaction of using VTC consultation system.
3. Determine physician satisfaction of using VTC consultation system.
4. Estimate cost savings of using VTC consultation system in place of traditional face-to-face consultation for follow-ups.

### TECHNICAL APPROACH

We hope to validate the use of inexpensive desktop VTC system connected at 384 kb connectivity to visually diagnose patients with findings from chronic hepatitis. Diagnostic concordance between in person evaluation vs. those performed using the VTC will be compared. Also, both patients and physicians will be surveyed for both level of experience with VTC and computer systems and satisfaction of such a system. Finally, for those patients on TDY from distant sites, we will collect monetary and time cost data for their visit to Walter Reed. There have been no modifications in methodology from the initial approved protocol.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no updates in the literature on the use of telemedicine in hepatitis. We have the equipment installed and connectivity completed among three VTC systems. We have enrolled and completed examinations on 32 patients thus far. We have had no adverse events, and no patients have withdrawn from our study.

The number of subjects enrolled to the study since last APR at WRAMC is 30 and the total enrolled to date at WRAMC is 32.

### CONCLUSIONS

Physical exams using VTC appear to strongly agree with in-person examinations with high kappa agreement scores. Patients positively rated the experience, and the majority preferred VTC to traveling long distances to see the physicians. Findings that require depth perception (e.g. gynecomastia), fine detail (e.g. rash) and those requiring subtle color discrimination (e.g. jaundice) may be difficult to detect consistently by VTC.

## DETAIL SUMMARY SHEET

**TITLE:** A Randomized Multicenter Trial Comparing Induction PEG Intron-A Plus Ribavirin Versus PEG-Intron A in Patients Who Have Previously Not Responded or Have Relapsed Following Intron-A Based Therapy for Chronic Hepatitis C, With Maintenance Therapy for Patients Who Continue to Remain Non-Responsive

**KEYWORDS:** Hepatitis C, Interferon, Ribavirin

**PRINCIPAL INVESTIGATOR:** Holtzmuller, Kent COL MC

**DEPARTMENT:** Medicine

**STATUS:** C

**SERVICE:** Gastroenterology

**INITIAL APPROVAL DATE:** 18 July 2000

### STUDY OBJECTIVE:

The primary objective of this study is to evaluate the efficacy of pegylated interferon alfa- 2b and ribavirin in patients with hepatitis C who have previously failed an interferon based protocol.

### TECHNICAL APPROACH:

There have been no modifications to the protocol design. 20 patients to a total of 40 have increased the number of patients that WRAMC is allowed to enter into the study. This is an open label trial where HCV patients who have previously been treated with interferon based anti-viral therapy are treated with pegylated interferon alfa-2b and ribavirin for 48 weeks. The patients are randomized to pegylated interferon alfa-2b 1.5 mcg/kg/week + ribavirin 1000-1200 mg/day for 12 weeks followed by pegylated interferon alfa-2b 1.0 mcg/kg + ribavirin 800 mg/day for 36 weeks or pegylated interferon alfa-2b 1.0 mcg/kg + ribavirin 800 mg/day for 48 weeks.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Interim results suggest the use of induction dosing does not improve the SVR in the groups evaluated. Previous combination nonresponders achieve a sustained response in 5-10% of participants.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 23. The total number enrolled study-wide is 728, if multi-site study.

### CONCLUSIONS

None.

## DETAIL SUMMARY SHEET

TITLE: CALGB 49906 - A Phase III Study of Doxorubicin-Cyclophosphamide Therapy Followed by Paclitaxel or Docetaxel Given Weekly or Every Three Weeks in Patients With Axillary Node-Positive Breast Cancer

KEYWORDS: Node Positive, Breast Cancer; Paclitaxel vs. Docetaxel

PRINCIPAL INVESTIGATOR: COL Joseph J. Drabick MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 25 January 2000

### STUDY OBJECTIVE

To determine whether Docetaxel improves disease-free survival and overall survival when compared to paclitaxel following four cycles of doxorubicin-cyclophosphamide therapy for women with node-positive breast cancer. To determine whether weekly administration of taxane (paclitaxel or Docetaxel) for 12 weeks improves disease-free survival and overall survival when compared with conventional (every three weeks) schedule for four cycles following four cycles of doxorubicin-cyclophosphamide therapy. To compare the toxicity of both drugs, Docetaxel and paclitaxel, given in the weekly or every three-week cycles.

### TECHNICAL APPROACH

All eligible patients will be randomized to one of four possible treatment arms (A, B, C, or D). All patients will initially receive four cycles of doxorubicin-cyclophosphamide. Subsequent treatment will be according to randomization. Treatment A: Paclitaxel will be given over three hours every three weeks x four cycles. Treatment B: Paclitaxel will be given over one hour every three weeks x 12 weeks. Treatment C: Docetaxel will be given over one hour every three weeks x four cycles. Treatment D: Docetaxel will be given over one hour every week x 12 weeks. Following chemotherapy, all patients with positive estrogen receptors will be given oral Tamoxifen for five years.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been no publications reporting data.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 4. The total number enrolled study-wide is 5059, if multi-site study. Grade 4 toxicities have been reported. Adverse events were reported 9 October 2001 and 8 November 2001. Study was closed to accrual 8 January 2002.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 159806 - ERBB-2 and P53 in response and Outcome After Paclitaxel Chemotherapy for Metastatic Breast Cancer

KEYWORDS: Erb-B-2, p53, paclitaxel, metastatic breast cancer

PRINCIPAL INVESTIGATOR: Joseph P. Drabick COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 09 May 2000

### STUDY OBJECTIVE

To correlate the growth factor receptor ErbB-2 and p53 with response rate, time to progression, and overall survival of patients with metastatic breast cancer treated with paclitaxel on CALGB 9342. To determine if amplification and over-expression of ErbB-2 must be present in order to predict response to paclitaxel.

### TECHNICAL APPROACH

Primary tissue from patients enrolled on CALGB 9342 will be used for histopathological evaluation, immunohistochemical evaluation, FISH, sequence analysis, p53 analysis and genomic sequencing will be done. The methods for assessing ErbB-2 and p53 will be correlated.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review last year there have been no publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 5. The total number enrolled study-wide is 188, if multi-site study. This study involves tissue block submission.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.



## DETAIL SUMMARY SHEET

**TITLE:** CALGB 89803 - A Phase III Intergroup Trial of Irinotecan (CPT-11) (NSC #6163480) Plus Fluorouracil/Leucovorin (5-FU/LV) Versus Leucovorin/Leucovorin Alone After Curative Resection for Patients with Stage III Colon Cancer.

**KEYWORDS:** Colon Cancer; Stage III; Irinotecan (CPT-11); Fluorouracil/Leucovorin (5FU/LV)

**PRINCIPAL INVESTIGATOR:** Joseph Drabick, COL MC  
**ASSOCIATES:**

**DEPARTMENT:** Medicine  
**SERVICE:** Hematology-Oncology

**STATUS:** O  
**INITIAL APPROVAL DATE:** 25 July 2000

### STUDY OBJECTIVES:

To determine if the addition of CPT-11 to the standard 5FU/LV treatment improves overall and disease free survival in Stage III colon cancer patients after curative resection.

### TECHNICAL APPROACH

Eligible patients will be randomized to one of two treatment regimens. Treatment A is the standard adjuvant treatment with 5FU and Leucovorin (LV) which is given weekly for 6 weeks followed by two rest weeks repeated times four cycles. Treatment B is the addition of CPT-11 to 5FU/LV, which is given weekly for four weeks followed by two rest weeks repeated times five cycles. A CBC and Chemistries will be done every treatment week. After therapy is completed the patient will be observed for recurrence. Follow-up will include physical exams, lab-work and chest x-rays. Other follow-up exams, such as CT scans, will be PRN.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting any data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 3. The total number enrolled study-wide is 1264, if multi-site study. Grade 4 toxicities include 53 neutrophils/granulocytes (ANC), 16 leukocytes (total WBC), 1 hemoglobin (Hgb), 1 platelets, 1 supraventricular arrhythmias, 2 hypotension, 3 cardiac-ischemia/infarction, 14 thrombosis/embolism, 8 fatigue (lethargy/malaise), 1 weight loss, 4 anorexia, 6 nausea, 1 stomatitis/pharyngitis (oral), 5 dehydration, 1 constipation, 7 vomiting, 23 diarrhea (w/o colostomy), 1 GI-other, 1 bilirubin, 3 infection w/o neutropenia, 1 catheter-related infection, 3 febrile neutropenia (fever), 2 infection/other, 3 hypophosphatemia, 1 hypophosphatemia, 2 hyperglycemia, 2 CNS cerebrovascular ischemia, 5 abdominal pain or cramping, 1 chest pain (non-cardiac), 1 dyspnea (shortness of breath), 3 pleural effusion (non-malignant), 1 pulmonary fibrosis, 1 adult respiratory distress syn, 1 hypoxia, and 1 creatinine. Grade 5 toxicities include 7 neutrophils/granulocytes (ANC), 2 cardiac-ischemia/infarction, 2 thrombosis/embolism, 2 circulatory or cardiac-other, 1 diarrhea (w/o colostomy), 3 GI-other, 1 infection w/unknown ANC, 1 CNS cerebrovascular ischemia, and 1 pulmonary-other. Adverse event reported April 5, 2001. This study was closed to accrual effective May 15, 2001.

Ref: CALGB Statistical Report

### CONCLUSIONS

No conclusions have been reached.

## DETAIL SUMMARY SHEET

TITLE: CALGB 19901 - Phase II Study of Fludarabine Induction Followed by Campath-1 H Consolidation in Untreated Patients with Chronic Lymphocytic Leukemia

KEYWORDS: Phase II; Fludarabine; Campath-1H; Chronic Lymphocytic Leukemia

PRINCIPAL INVESTIGATOR: Joseph Drabick, COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 25 July 2000

### STUDY OBJECTIVE:

To determine the overall complete response rate, the infectious toxicities, the progression-free and overall survival and the immunologic effects of sequential treatment with fludarabine and Campath-1H in previously untreated patients with active chronic lymphocytic leukemia.

### TECHNICAL APPROACH

INDUCTION with Fludarabine is to be given five days per week during weeks 1,5,9 and 13 (a total of four 28 day cycles). Two months later, CONSOLIDATION with Campath-1H is to be given three times per week for six weeks. Restaging bone marrows will be done after INDUCTION, before CONSOLIDATION, at the end of CONSOLIDATION and two months after CONSOLIDATION.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been one abstract published since this study's review last year.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 86, if multi-site study. Grade 4 toxicities include 1 neutrophils/granulocytes (ANC). Adverse events reported January 16, 2001, and April 20, 2001. This study was closed to accrual effective February 28, 2002.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 99808 - Docetaxel and Estramustine Versus Mitoxantrone and Prednisone for Advanced, Hormone Refractory Prostate Cancer, Phase III

KEYWORDS: Advanced Hormone Refractory Prostate Cancer; Docetaxel; Estramustine; Mitoxantrone; Prednisone; Phase III

PRINCIPAL INVESTIGATOR: Drabick, Joseph J. COL MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 18 September 2000

### STUDY OBJECTIVE

To compare overall survival and progression-free survival in patients with hormone refractory metastatic prostate cancer, Stage D1 or D2, who are randomized either to treatment Arm 1, estramustine + docetaxel, or Arm 2, Mitoxantrone and prednisone. To compare the toxicities between the two study arms. To evaluate Quality of Life. To record PSA values for future correlations with response and survival. To compare responses between the two treatment groups.

### TECHNICAL APPROACH

Eligible patients will be randomized to ARM 1 or ARM 2. Patients in ARM 1 will receive estramustine orally, three times per day on days 1 and 2, will receive docetaxel IV on day 2, and 3 doses of dexamethasone prior to receiving docetaxel. ARM 1 will be given every 21 days. All patients will take low dose enteric-coated aspirin, 325 mg, orally, daily for anticoagulation therapy. A maximum of 12 cycles will be given. If no toxicity occurs during cycle 1 the dose of docetaxel will be escalated. If significant toxicity occurs, the dose of docetaxel will be reduced. Additionally, all patients will require additional prophylaxis against arterial events. One of the following 3 anticoagulants are to be used -- coumadin, levenox, or fragmin in addition to the aspirin. Patients on ARM 2 will receive Mitoxantrone, IV, on day 1 and prednisone orally twice a day on days 1 to 21. ARM 2 will be given every 21 days. A maximum of 12 cycles will be given. If no toxicity occurs during cycle 1, the Mitoxantrone dose will be escalated. If, after a dose, escalation of significant toxicities occurs, the dose of Mitoxantrone will be reduced.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data from this or other studies with similar design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 770, if multi-site study. Grade 4 toxicities include 12 cardiovascular, 2 flu-like symptoms, 7 gastrointestinal, 60 hematologic, 3 hemorrhage, 6 infection, 2 liver, 3 lung, 3 metabolic, 2 neurologic, and 3 pain. Grade 5 toxicities include 3 ADR, 1 hematologic, 1 hemorrhage, 2 infections, 1 liver, 2 lung, and 1 renal/bladder. No adverse events reported. This study was closed to accrual effective January 15, 2003.

Ref: CALGB Statistical Report July 2003

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 9764 - Genetic Changes in Diffuse Aggressive Non-Hodgkin's Lymphoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 19 September 2000

### STUDY OBJECTIVE:

To estimate the proportions of patients with rearrangements affecting the MYC, BCL2, and BCL6 genes determined by FISH, overtly amplified chromosomal regions and non-random copy number changes of chromosomal regions determined by CGH. To investigate the prognostic importance of these genetic markers by studying their relationships with the clinical outcomes: response to therapy, failure-free survival (FFS), and overall survival (OS) (response to therapy). To investigate the interrelationships among these genetic and biological markers and their relationships with clinical features of the disease, such as disease site (nodal vs. extranodal) and stage of disease.

### TECHNICAL APPROACH:

There is a retrospective and prospective component. The retrospective component is for patients who were enrolled on CALGB 8852 and CALGB 9351. They are eligible if tissue blocks obtained at diagnosis and at time of refractory/relapsed NHL are available for submission to the CALGB Pathology Coordinating Office (PCO), at the Ohio State University, B054 Graves Hall, 333 West 10<sup>th</sup> Avenue, Columbus, Ohio 43210-1239 and to Memorial Sloan-Kettering Cancer Center, Department of Human Genetics, 1275 York Avenue, NYC 10021. Only blocks from subjects who are still living will be collected. No consent form is required for the retrospective component.

The prospective component requires that consent be obtained from patients who are being treated for NHL on a CALGB treatment study. Participation in this study is not mandatory for participation in a CALGB treatment study. A Research Coordinator/Nurse will obtain tissue blocks from the Pathology Departments. When the above institutions receive the tissue blocks, a Unique Patient Number (UPN) will be assigned to each patient's blocks to protect the patient's identity.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this study or other studies with similar design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 96, if multi-site study. No toxicities reported. Ref: CALGB Statistical Report July 2003.

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: Prospective Evaluation of Fatigue in Patients with Chronic B-Cell Chronic Lymphocytic Leukemia

KEYWORDS: Fatigue, Chronic Leukemia

PRINCIPAL INVESTIGATOR: CPT Amanda M. Bell, MC MD

ASSOCIATES: CPT Joseph Flynn, DO; MAJ John Byrd, MD; Magaret Lucas, PA-C; Kathy Park, RN

DEPARTMENT: Medicine

STATUS: C

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 18 January 2000

### STUDY OBJECTIVE

1. To evaluate fatigue experienced by Chronic Lymphocytic Leukemia (CLL) patients as compared to that experienced by matched members of the general medical population.
2. To evaluate the relationship between fatigue and disease stage of CLL.
3. To evaluate the progression of fatigue over time in patients with untreated CLL.
4. To evaluate the relationship of response to therapy and fatigue in CLL patients.
5. To determine if there is a correlation with cytokines and fatigue experienced by CLL patients.
6. To evaluate the overall quality of life experienced by CLL patients as compared to that experienced by the general medical population.

### TECHNICAL APPROACH

Patient with CLL will be enrolled into one of three study groups. Cohort 1 is a prospective, case controlled study of fatigue in CLL. Cohort 2 is a cross sectional study when compared with Cohort 1 to detect changes in fatigue related to treatment status. Treatment status includes standard treatment, alkylator therapy, fludarabine, and fludarabine refractory. Cohort 3 is a longitudinal assessment of fatigue over time in patients receiving treatment. After enrollment, all cohorts will fill out a questionnaire with age, sex, date of CLL diagnosis, current disease stage, current medications, treatment received for CLL, and current medical conditions other than CLL. A CBC and B2 microglobulin level will be drawn. All patients will fill out the FACT-An/F scale with assistance from the investigator. Cohort 1 will do this at the beginning, at six months and at study completion in one year. Cohort 2 will do this at the beginning. Cohort 3 will do this at treatment initiation, mid-cycle in their treatment, and at one month after treatment. The control group will be recruited from the resident panels in the General Internal Medicine clinic after the CLL patients are registered in order to match underlying medical problems. They will fill out the same data in the questionnaire with the exception of the CLL questions. A CBC will be drawn at the beginning and end of the study, and patients will fill out the FACT-An/F scale at the beginning, middle, and end of the study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 11. The total number enrolled study-wide is 11, if multi-site study.

### CONCLUSIONS

Study terminated due to lack of available staff.

## DETAIL SUMMARY SHEET

**TITLE:** A Phase II Evaluation of Rubitecan, A Novel Oral Topoisomerase I Inhibitor, in Newly Diagnosed, Recurrent, and Refractory Multiple Myeloma

**KEYWORDS:** myeloma, rubitecan

**PRINCIPAL INVESTIGATOR:** Joseph J. Drabick COL MC

**ASSOCIATES:** Carl Willis MAJ MC

**DEPARTMENT:** Medicine

**STATUS:** C

**SERVICE:** Hematology-Oncology

**INITIAL APPROVAL DATE:** 8 February 2000

### STUDY OBJECTIVE

The purpose of this phase II study is to determine if rubitecan, an oral topoisomerase I inhibitor, has clinical activity in patients with recurrent, refractory, or newly diagnosed multiple myeloma.

### TECHNICAL APPROACH

The structure of the protocol has not been changed to date. Patients found to be eligible are treated with oral rubitecan according to prior treatment status. Patients will receive rubitecan as a single oral dose in the morning, Monday-Friday, with a rest on Saturday and Sunday. Patients are evaluated at two-week intervals for toxicity and at monthly intervals for activity. Dose may be modified according to toxicity or lack thereof. Patients will continue on treatment until there is evidence of progression of myeloma or toxicity.

### PRIOR AND CURRENT PROGRESS

Five patients have been enrolled on this study at WRAMC. Four SAEs have been submitted. The first of these was for a patient who experienced ARF, with the rubitecan possibly contributing to this problem. Patient was also found to have pyelonephritis, BPH, and urosepsis. The second SAE reported was for mental status changes, probably not related to study drug. The last two SAEs were also for acute renal failure, not felt to be related to study drug. The best response seen on this study was one complete response, which was short-lived. This drug is not yet approved by the FDA for any clinical indication. It is being studied in some hematological malignancies and many solid tumors.

The number of subjects enrolled to the study since last APR at WRAMC is 2 and the total enrolled to date at WRAMC is 5.

### CONCLUSIONS

This protocol has been closed, as there has only been one short-lived response.

## DETAIL SUMMARY SHEET

**TITLE:** Does Use of a Temporary Silencer Adjustable Airway Dilator Predict Outcome Using Permanent Silencer Adjustable Airway Dilator in Treatment of Obstructive Sleep Apnea?

**KEYWORDS:** OSA, temporary oral appliance, permanent oral appliance

**PRINCIPAL INVESTIGATOR:** Kristo, David MAJ MC

**ASSOCIATES:** Teotima Andrada MS RPSGT, Paula Ephraim, LTC, AN (Ret.), MSN, RN; LTC Kevin McGlynn DDS, Robin Howard MA, David Bitonti DMd CDR DC USN, Scott A. Synnott DDS CPT DC USN

**DEPARTMENT:** Medicine

**STATUS:** C

**SERVICE:** Pulmonary & Critical Care Medicine

**INITIAL APPROVAL DATE:** 28 March 2000

### STUDY OBJECTIVE

To determine whether a Silencer adjustable temporary airway dilator (AD) is predictive of outcome of a permanent Silencer adjustable airway dilator in treating obstructive sleep apnea (OSA).

### TECHNICAL APPROACH

Subjects receive acoustic three-dimensional assessment of the airway, are given a temporary airway dilator to wear for two weeks, and then undergo a sleep study with the temporary AD. Next, subjects are given a permanent AD, wear it for six weeks and undergo a sleep study with the permanent AD. This study will examine whether a strong correlation exists between successful treatment of OSAHS with the temporary AD and successful treatment with the permanent AD. Additionally, the acoustic airway measurements will be examined to see if they have predictive value.

### PRIOR AND CURRENT PROGRESS

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 25. As reported in the 2002 APR, fourteen were studied incorrectly; they received temporary airway dilator treatment in a neutral position (no mandibular advancement). Additionally, the permanent airway dilator, which was fabricated in Canada, was not optimally positioned in up to nine patients. In addition to these fourteen patients, six patients did not receive a sleep study, and five patients were dropouts. Reasons for dropouts were fully explained in previous APR. Plans to follow-up enrolled subjects and correct study procedures for 25 new subjects were detailed and approved in an addendum dated 29 November 2001. Follow-ups for enrolled subjects were completed as specified in the addendum. No other activity whatsoever has occurred regarding this protocol in the last year, largely due to the non-availability of the designer and expert on this variety of oral appliance. Based on reports of his serious illness, difficulty in contacting him, and the lack of a replacement to perform his role in the study, it has been decided to terminate this study.

### CONCLUSIONS

No conclusions will be drawn from this study.

## DETAIL SUMMARY SHEET

**TITLE:** A Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Safety and Efficacy of 12 Weeks of 2 Oral Doses (200 mg and 400 mg Once Daily) of PROVIGIL (Modafinil) as Treatment for Adults with Excessive Daytime Sleepiness Associated with Obstructive Sleep Apnea/Hypopnea Syndrome Followed by a 12-Month Open-Label Extension

**KEYWORDS:** Provigil, Modafinil, sleepiness, OSA, CPAP

**PRINCIPAL INVESTIGATOR:** Kristo, David MAJ MC

**ASSOCIATES:** COL Arn Eliasson MC; Yvonne Taylor RN MSN CNP; Tim Andrada MS

**DEPARTMENT:** Medicine

**STATUS:** C

**SERVICE:** Pulmonary & Critical Care Medicine

**INITIAL APPROVAL DATE:** 28 March 2000

### STUDY OBJECTIVE

The objectives of this study are to determine the safety and efficacy of PROVIGIL 200 mg/day (once in the morning) and 400 mg/day (once in the morning) as a treatment for excessive daytime sleepiness (EDS) in patients with obstructive sleep apnea/hypopnea syndrome (OSAHS) who need nasal continuous positive airway pressure (CPAP), and who have been characterized with regard to their actual CPAP use patterns. The primary efficacy objective will be tested by comparing the change from baseline to week 12 (or endpoint) in the Maintenance of Wakefulness Test and the Clinical Global Impression Scale between the group treated with PROVIGIL 400 mg/day and the placebo-treated group. (Note: previously, the Epworth Sleepiness Scale was the primary efficacy objective.)

### TECHNICAL APPROACH

Patients using CPAP who are still experiencing excessive daytime sleepiness will be extensively screened to exclude variables such as concomitant sleep disorders, acute illness, prior Modafinil use, use of medications that might interact with Modafinil, etc. After initial screening, patients will undergo at-home CPAP testing for 2 nights to insure that their CPAP titration level is adequate to treat their OSAHS. They will also undergo 14 nights of at-home CPAP testing to insure that they do have at least partial CPAP compliance. Patients who pass all of the above screening procedures are then randomized (1:1:1) to receive PROVIGIL 200 mg/day or 400 mg/day or placebo for one 12-week period. During this period, they are seen once a month for a variety of procedures, including EKG, blood labs, Maintenance of Wakefulness tests, questionnaires, etc. After completing at least 8 week of double-blind treatment, patients are eligible of an optional 12 months of open label treatment with Modafinil.

### PRIOR AND CURRENT PROGRESS

Five subjects were enrolled at WRAMC. Since the last APR, no subjects have been enrolled. Three subjects completed the open-label portion of the study. There were no serious adverse events for any WRAMC participants.

After all WRAMC subjects had completed participation in this study, Cephalon reported a serious adverse event in another study involving Modafinil, in which a child died following treatment for ADHD. The report indicated the child experienced suicidal ideation. The report was sent to DCI with notification of a possible FDA audit of all of Cephalon's research sites. Representatives from DCI performed a site review of 00-1702 study documents on 24 October 2002, and found the records adequate, and only in need of some reorganization.

### CONCLUSIONS

Cephalon is currently verifying all study data, and has not yet published findings.



## DETAIL SUMMARY SHEET

TITLE: Development of HIV Specific CD<sup>+</sup> T Cells

KEYWORDS: HIV, T Cell Lines

PRINCIPAL INVESTIGATOR: COL Naomi Aronson  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Infectious Disease

STATUS: O  
INITIAL APPROVAL DATE: 26 October 1999

### STUDY OBJECTIVE

Compare epitope recognition between HIV negative individuals vaccinated with gp160 MN/LAI and HIV infected individuals 2. Generate *Pneumocystis carini* specific CD4<sup>+</sup>T cell lines to assess the clonal deletion in disease progression 3. Generate *Candida albicans* specific T cell lines from archived samples.

### TECHNICAL APPROACH

Six HIV infected patients WR stage 1, 2 with CD4>400 and no history of gp160 immunization, six HIV infected patients with CD4 50-200, and twelve HIV infected patients with archived PMBC in the HIV repository from past times that they were not Candida anergic who are now Candida anergic will be enrolled. GP 160, Pneumocystis, Candida specific T-cells will be developed. Proliferation assays, T-cell repertoire by BV gene analysis and spectratyping will be performed. Addendum for modify third objective to generate HIV gp 160 specific cell lines from archival samples in subjects who received gp 160 but have lost proliferation responses.

### PRIOR AND CURRENT PROGRESS

Recent literature shows research to be unique. Six subjects have been enrolled in the first phase looking at gp 160 envelope recognition in HIV patients with CD4>400 as compared to HIV uninfected gp 160 vaccine recipients from another WRAIR protocol. In 4/6 T cell lines specific for gp 160 were able to be proliferated. Six subjects were enrolled in the second phase of the study, generating Pc (pneumocystis) specific T cell lines in HIV infected patients with depleted (50-200) CD4 counts. 4/6 permitted expansion of T cell lines. In the third phase of the study, six subjects have been enrolled. Two were found to have high gp 160 lymphocyte stimulation indices so cell lines were not initiated. 3/4 subjects had gp 160 specific cell lines from archived cells generated. There have been no adverse events and no early withdrawals. This is a single site study. This is a laboratory study and there is not direct benefit for the participants.

The number of subjects enrolled to the study since last APR at WRAMC is six and the total enrolled to date at WRAMC is seventeen. (One subject enrolled in two arms; no additional blood drawn so counted as one enrollment.)

### CONCLUSIONS

Comparison of epitope reactivity of T helper response induced by HIV gp 160 vaccine as compared to gp 160 specific T cell lines from chronically infected HIV patients with CD>400 showed some differences. Vaccinated HIV negative subjects showed strong and broad responses scattered across the envelope sequence. In contrast, HIV infected patients had poor reactivity to HIV envelope in breadth and amplitude. Laboratory investigations of the pneumocystis specific cell lines are in progress. Gp 160 specific T cells were able to be generated from frozen archived PBMC in the third phase of study.

## DETAIL SUMMARY SHEET

TITLE: Cytotoxic T Lymphocyte Recognition of Epithelial Cancers

KEYWORDS: Cytotoxic; T Lymphocyte; Epithelial Cancers

PRINCIPAL INVESTIGATOR: LTC George E. Peoples MC / LTC (P) Craig Shriver MC (acting)

ASSOCIATES: CPT Gayle Ryan MC; CPT Bryan Fisk MC; Dr. Vasantha Srikantan

DEPARTMENT: Surgery

STATUS: O

SERVICE: General Surgery

INITIAL APPROVAL DATE: 4 April 2000

### STUDY OBJECTIVE

To collect discarded tissue, blood, and body fluids in order to investigate the cellular immune response to epithelial cancers in order to identify common tumor antigens that may serve as the target of immunotherapeutics such as vaccines.

### TECHNICAL APPROACH

Patients with known epithelial malignancies such as ovarian, breast, lung and prostate who are having blood drawn, malignant pleural effusions or ascites removed, or surgical removals of large tumors are identified by their providers. These providers contact us to inform us of tissue or body fluids that are to be discarded. Prostate patients who have been enrolled in the serum bank CPDR trial have been identified since the cellular components of their blood draw are discarded. The patients are consented unless the samples are collected without patient identification. The lymphocytes and/or tumor cells are isolated and stored for future studies.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Review of recent literature reveals no new findings in this field.

We have not enrolled any new patients into this study since the last APR. We want to keep this protocol open in order to assess the feasibility of investigating the use of peptide cancer vaccine immunotherapy as an adjuvant to surgical and chemotherapy of lung cancer. No consented patient has asked for sample to be removed from study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 48.

### CONCLUSIONS

There are no new conclusions since the last APR.

## DETAIL SUMMARY SHEET

TITLE: Pressor Effects of Hemoglobin Based Oxygen Carrying Solution in Human Blood Vessels

PRINCIPAL INVESTIGATOR: Mongan, Paul LTC MC

DEPARTMENT: Surgery

STATUS: T

SERVICE: Anesthesia-Operative

INITIAL APPROVAL DATE: 7 March 2000

### STUDY OBJECTIVE:

The aim of this study is to determine the effects of hemoglobin-based oxygen-carrying solutions (HBOCs) on human blood vessels.

### TECHNICAL APPROACH:

After surgical resection of the specimen, a small portion (1.5") of vessels that will be discarded will be taken from the specimen before its transfer to anatomic pathology. No tissue will be taken if its absence would alter the pathological reading of the specimen or potentially obscure the diagnosis. The use of the tissue at Uniformed Services University of the Health Sciences is not a standard part of patient care at USUHS and is thus research. The specimen will be placed in Krebs solution and transported to the Department of Anesthesiology research laboratory at USUHS by the PI or his designee. Vessels will be prepared and tested using routine vessel ring methodology in our laboratory. In brief, the vessels will be cleaned of excessive adherent tissue, with care being taken not to damage either the vascular endothelium or surrounding neurons in the adventitia. Blood vessels will then be cut into rings (4-5 mm in length). Multiple rings from each vessel will be tested simultaneously. These rings will be placed on stainless steel hooks and lowered into water-jacketed organ baths maintained at 37°C and filled with Krebs-Ringer solution of the following composition (in mM); NaCl, 119; KCl, 4.7; CaCl<sub>2</sub>, 2.5; KH<sub>2</sub>PO<sub>4</sub>, 1.2; MgSO<sub>4</sub>, 1.2; NaHCO<sub>3</sub>, 25; and glucose, 5.6. Each vessel will be stretched to its optimal length as determined by the tension response to serotonin (5-HT) measured by a Grass FT10 force transducer. After a 90 min equilibration period, phenylephrine (PE) or 5HT concentration response relationships will be determined. After washing and return to basal tension, vessels will be contracted with increasing concentrations of HBOCs (10<sup>-8</sup>M to 6x10<sup>-6</sup> M). Data will be expressed as a percent of the maximum tension developed in response to a maximum effective dose of PE or 5-HT. To determine the endothelial independent activity of the HBOCs, we will remove the endothelium by gently scraping the luminal wall of the blood vessel. The effectiveness of the removal of functional endothelium will be verified by the absence of a relaxant response to acetylcholine (Ach, 10<sup>-6</sup>M). These scraped rings will then be used to examine the direct actions of HBOCs on vascular smooth muscle activity. Clarification of the mechanism of changes in tension related to the HBOC will be done by incubating the vessel rings with specific blockers of nitric oxides synthase, soluble guanyl cyclase, endothelial phosphodiesterase, endothelin, cAMP, IP<sub>3</sub>, pathways and KATP channels. After study, excess tissue will be appropriately disposed of as medical waste according to USUHS guidelines. Genetic testing will not be done.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE:

No progress in past year due to inability to procure additional equipment. No enrollment at WRAMC.

### CONCLUSIONS:

Study terminated. No conclusions to report. The lack of institutional commitment by WRAMC and/or USUHS to purchase equipment made for lack of progress on this project.

## DETAIL SUMMARY SHEET

TITLE: Sentinel Lymph Node (SLN) Evaluation in Colorectal Cancer (CRC)

KEYWORDS: metastatic colorectal cancer, sentinel lymph node (SLN)

PRINCIPAL INVESTIGATOR: LTC George E. Peoples MC

ASSOCIATES: COL Daniel Otchy MC; COL Craig Shriver MC; LTC Carol Adair MC; MAJ Darin Cox MC; CPT Dwight Kellicut MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: General Surgery

INITIAL APPROVAL DATE: 18 April 2000

### STUDY OBJECTIVE

To determine the feasibility and usefulness of sentinel lymph node (SLN) biopsy in colorectal cancer (CRC).

### TECHNICAL APPROACH

The surgery performed for these patients is standard. The blue dye is injected intramurally around the tumor either in vivo or ex vivo. The blue nodes are labeled as sentinel and submitted separately to pathology.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The protocol is still open.

The number of subjects enrolled to the study since last APR at WRAMC is 3 and total enrolled to date at WRAMC is 20. A literature review revealed no new information on this topic. No adverse events were experienced.

### CONCLUSIONS

The SLN technique is feasible and would appear to improve staging in CRC from our limited preliminary results.

## DETAIL SUMMARY SHEET

TITLE: Evaluation of Neutrophil Activation in Diabetes After Carotid Endarterectomy

PRINCIPAL INVESTIGATOR: CPT Scott Rehrig MC

ASSOCIATES: David Gillespie, LTC MC

DEPARTMENT: Surgery

SERVICE: General Surgery

STATUS: (O) Abeyance

INITIAL APPROVAL DATE: 18 April 2000

### STUDY OBJECTIVE

Diabetes is a known risk factor for increased morbidity and mortality following most surgical procedures and traumatic injuries. The primary hypothesis in this study is that in diabetes surgical intervention alone alters the neutrophil (PMN)-endothelial cell interaction, which may play a role in the increased organ injury observed in these patients. The aim of this study is to evaluate the effect of non-insulin dependent (NIDDM) diabetes on neutrophil cell adhesion molecule expression and hydrogen peroxide production in the context of a surgical procedure.

### TECHNICAL APPROACH

Patients were informed of the protocol and consented prior to their operation. Patients served as their own controls. Preoperative blood was collected prior to procedure through an indwelling line placed for the purpose of intraoperative monitoring. A second blood draw was obtained intraoperatively via the same indwelling catheter one hour after skin incision. The third and final collection was obtained within twenty minutes upon arrival to post anesthesia care unit, via indwelling catheter. The samples were then transported to USUHS at room temperature. Red blood cells were lysed using 1x lysis buffer for twenty minutes. The samples were then centrifuged, red cells decanted, and the neutrophil pellets were washed in buffered saline. To determine expression of CD18 and CD11b, the isolated neutrophils were exposed to anti-human CD18 and CD11b antibody for fifteen minutes on ice. The amount of hydrogen peroxide produced by neutrophils was then maximally stimulated oxidative burst. After incubation, the cells were rewashed and suspended in PBS for flow cytometric analysis. The neutrophils were identified on forward and right angle scatter of a 488nm argon laser on an EPICS XL. The cellular fluorescence of each of three measures (DCF, CD11b, and CD18) were measured with logarithmic amplification and expressed as percent positive cells compared to cells stained with isotype control antibody.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

None.

### CONCLUSIONS

Study is currently on hold until new PI returns from overseas commitment.

## DETAIL SUMMARY SHEET

TITLE: Phase 1b Trial of HER-2/neu Peptide (E75) Vaccine in Patients at High Risk for Recurrence after Surgical Extirpation of Prostate Cancer

KEYWORDS: Vaccine, Her2 neu, prostate cancer

PRINCIPAL INVESTIGATOR: LTC George E. Peoples MC/ COL Craig Shriver MC (acting)

ASSOCIATES: COL David McLeod MC, COL Judd Moul MC

DEPARTMENT: Surgery

SERVICE: General Surgery

STATUS: O

INITIAL APPROVAL DATE: 23 May 2000

### STUDY OBJECTIVE

- 1) Assess safety and document local and systemic toxicity to the peptide vaccine (E75+ GM-CSF).
- 2) Determine maximum tolerated dose (MTD) and optimal biologic dose (OBD) for the peptide vaccine.
- 3) Evaluate the in vivo cellular immune response to the peptide vaccine.
- 4) Evaluate time to recurrence in the vaccinated patients vs. matched controls.

### TECHNICAL APPROACH

Eligible patients are identified and offered study participation after referral from their urologist. Consenting patients are tested for HLA A2 type: A2+ patients receive vaccine; A2- patients are observed clinically q3 months for 18 months. Patients assigned to vaccine are skin tested to assess immunologic intactness and then vaccinated q 3 to 4 weeks x 6 with blood draw before each vaccine to assess peptide-specific immune response. Patients are observed with serial vital signs for one hour after each vaccine and at 48 hours for delayed hypersensitivity reaction. Vaccinated patients return for a final blood test and skin test four weeks after series is complete, and followed clinically q3 months for 18 months. Vaccine is given by intradermal injection 0.5 cc x 2 with a dose escalation scheme for three patients at 100 mcg of peptide, three patients at 500 mcg of peptide, and three at 1000 mcg of peptide - with this dose for remaining patients if well tolerated. This study was amended to add FDA administrative changes and to add a group of intermediate risk patients thus expanding enrollment. The protocol and consent form have been amended to allow appropriate photography of DTH responses as well as of local and diffuse skin reactions to the vaccine.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Review of current literature reveals little new information, and nothing that has an effect on the direction of this study. No benefit to study patients has been determined. Dimer Assay: We tested and implemented the HLA-A2 dimer assay as a means to monitor the in vivo immune response to peptide vaccinations. The dimer assay showed good correlation with standard immunologic assays and has become part of our standard battery of immunologic tests for our patients receiving E75 peptide vaccination. Dose escalation has been completed. Adjustment to vaccination schedule is now being implemented. The number of subjects enrolled to the study since last APR at WRAMC is 7. The total enrolled to date at WRAMC is 30 (18 vaccinated, 11 on observation arm, one found ineligible due to finding of anergy after consent). One patient was withdrawn from further vaccination after an adverse reaction, but remained under study observation. One patient was withdrawn from study participation due to total anergy diagnosed after enrolling in the study. Five adverse events have occurred in this reporting period: four large local reactions (grade II-expected), and one flu type constitutional reaction (grade II-expected). Two of these were reported to the IRB and FDA. Then, at FDA request, Grade II reactions were held for APR report. No patients have suffered any sequelae from these reactions.

### CONCLUSIONS

No clinical conclusions have been reached.

## DETAIL SUMMARY SHEET

TITLE: Phase 1b Trial of HER-2/neu Peptide (E75) Vaccine in Breast Cancer Patients at High Risk for Recurrence after Surgical and Medical Therapies

KEYWORDS: Vaccine, Her2 neu, Breast cancer

PRINCIPAL INVESTIGATOR: LTC George E. Peoples MC; COL Craig Shriver MC (acting)

ASSOCIATES: COL Craig Shriver MC

DEPARTMENT: Surgery

SERVICE: General Surgery

STATUS: O

INITIAL APPROVAL DATE: 23 May 2000

### STUDY OBJECTIVE

- 1) Assess safety and document local and systemic toxicity to the peptide vaccine (E75).
- 2) Determine maximum tolerated dose (MTD) and optimal biologic dose (OBD) for the peptide vaccine.
- 3) Evaluate the in vivo cellular immune response to the peptide vaccine.
- 4) Evaluate time to recurrence in the vaccinated patients vs. matched controls.

### TECHNICAL APPROACH

Eligible patients are identified and offered study participation after referral from their oncologist or radiation oncologist. Consenting patients are tested for HLA A2 type: A2+ patients receive the vaccine; A2- patients are observed clinically Q3 months for 18 months. Patients assigned to vaccine are skin tested to assess immunologic intactness and then vaccinated q 3 to 4 weeks x 6 with blood draw before each vaccine to assess peptide-specific immune response. Patients are observed with serial vital signs for one hour after each vaccine and at 48 hours for delayed hypersensitivity reaction. Vaccinated patients return for a final blood test and skin test 4 weeks after series is complete, and then are followed clinically Q3 months for 18 months. Vaccine is given by intradermal injection 0.5 cc X 2 with a dose escalation scheme for 3 patients at 100 mcg of peptide, 3 patients at 500 mcg of peptide, and 3 at 1000 mcg of peptide -- with this dose for remaining patients if well tolerated. This study was amended to: 1) add FDA changes; 2) add a group of intermediate risk patients; and 3) clarify recruiting procedures and approve a telephone script and patient letter for use in patient recruiting. The protocol and consent form have been amended to allow appropriate photography of DTH skin test responses as well as of local and diffuse skin reactions to the vaccine.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Review of current literature reveals little new information, and nothing that has an effect on the direction of this study. No benefit to study patients has been determined.

Dimer Assay: We tested and implemented the HLA-A2 dimer assay as a means to monitor the in vivo immune response to peptide vaccinations. The dimer assay showed good correlation with standard immunologic assays and has become part of our standard battery of immunologic tests for our patients receiving E75 peptide vaccinations. Dose escalation has been completed. Adjustment to vaccination schedule is now being implemented. The number of subjects enrolled to the study since last APR at WRAMC is 9 and the total enrolled to date at WRAMC is 35 (13 vaccinated, 19 being observed, 2 pending assignment, 1 withdrew before assignment). The total number enrolled study-wide is 37, if multi-site study. One ADR was reported to IRB in this reporting period (Grade II-large local reaction - expected). Patient suffered no sequelae. At FDA request, further ADRs of less than Grade III and of an expected nature will be held for reporting with APR.

### CONCLUSIONS

No clinical conclusions have been reached.

## DETAIL SUMMARY SHEET

TITLE: Creation of a Retrospective and Prospective Database of Patients Evaluated and Treated for Breast Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Peoples, George E. LTC MC

ASSOCIATES: Shriver, Craig LTC (P) MC; Maniscalco-Theberge, Mary COL MC; Arciero, Cletus CPT MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: General Surgery

INITIAL APPROVAL DATE: 25 July 2000

### STUDY OBJECTIVE

1. To collect data beginning on DCI approval of this protocol on all patients 18 and older who present to the General Surgery clinic at WRAMC with breast cancer.
2. To utilize this database to analyze the diagnosis treatment and treatment outcomes for patients undergoing treatment for breast cancer. Analysis will include but not be limited to: risk factors for developing breast cancer, effectiveness of various modalities of treatment, risk of recurrence.

### TECHNICAL APPROACH

The patients are identified by the CBCP nurse case-managers in the Comprehensive Breast Center. These patients are counseled and consented to be a part of this prospective clinical database. The nurses and physicians seeing the patient collect the information on data forms; then CBCP data managers enter the data into the database. The patients are assigned unique CBCP numbers to protect their confidentiality. The identifier code is kept secured in the CBCP Director, Dr. Shriver's office. He is the only person having access to the code.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 91 and the total enrolled to date at WRAMC is 180. The total number enrolled study-wide is 210. There have been no adverse events and no patients have withdrawn from the study. A review of the literature revealed no publications within the last year reporting data from studies of a similar design.

### CONCLUSIONS

This protocol is ongoing.



## DETAIL SUMMARY SHEET

**TITLE:** Intraoperative Carotid Duplex: A Prospective Study of the Clinical Significance of Residual Defects Following Carotid Endarterectomy

**KEYWORDS:** intraoperative, carotid, duplex

**PRINCIPAL INVESTIGATOR:** LTC James M. Goff

**ASSOCIATES:** LTC Sean D. O'Donnell MC, LTC David L. Gillespie MC, MAJ Neal Hadro MC, Margaret Kidwell, RVT

**DEPARTMENT:** Surgery

**STATUS:** O

**SERVICE:** Peripheral Vascular Surgery

**INITIAL APPROVAL DATE:** 18 January 2000

### STUDY OBJECTIVE

To compare the rate of neurologic events, restenosis, reoperation and death in patients who undergo carotid endarterectomy and in whom: 1) the intraoperative carotid duplex is normal and no repair is performed, 2) the intraoperative carotid duplex shows a minimal abnormality that is not repaired, 3) the intraoperative duplex shows an abnormality that is repaired, and 4) the carotid artery was opened only once versus two or more times.

### TECHNICAL APPROACH

This is a prospective observational study. Patients who are eligible for carotid endarterectomy undergo the standard medical and preoperative evaluation to ensure that there are no contraindications to surgery. This includes a thorough history and physical, labs, x-rays, EKGs, and consultations as dictated by their medical condition. Once scheduled for surgery, they are approached regarding their willingness to participate in the study. Informed consent is obtained. A datasheet is initiated on the patient to record demographic data, risk factors for atherosclerotic vascular disease, history of chronic medical problems, and previous vascular surgery. In the operating room, the findings of the initial duplex, any further surgical management decision should the duplex be abnormal, findings if re-explored, number of times re-opened and final duplex findings prior to leaving the operating room are recorded.

The intraoperative carotid duplex is standardized as follows. An ATL HDI 3000 machine, with a 10 MHz CL-10-5 sterile probe and sterile gel or saline to obtain acoustic coupling is used, with the probe in direct contact with the artery, using an incident angle of 60 degrees. Care is taken to avoid the presence of bubbles between the probe and artery or pressure against the artery. B-mode is first used to longitudinally scan the CCA, beginning proximal to the proximal endpoint of the endarterectomy and continuing into the ICA as far as accessible. The proximal endpoint of the endarterectomy and the clamp site in the CCA are then examined longitudinally and in transverse views in B-mode, followed by color flow and spectral analysis and measurement of the peak systolic velocity. The distal endpoint and the clamp site in the ICA are examined next, in color and with spectral analysis, with measurement of the peak systolic and end diastolic velocities and particular attention paid to the presence of mosaicism, spectral broadening or lack of acoustic window. In the cases in which the presence of a prosthetic patch precludes direct visualization of the distal endpoint, the most proximal portion of the ICA distal to the patch will be examined. The ECA will then be examined in B-mode followed by spectral analysis and measurement of the peak systolic velocity. The velocities recorded will be those that are the highest within the area of interest. Color pictures are obtained of the CCA at the proximal endpoint, the ICA at the distal endpoint and of the proximal ECA. If a defect is identified, minor or major, its characteristics, namely dimensions, location and associated velocities, are recorded, and a photograph obtained. This is repeated each time that a defect is identified. If a defect is identified which requires reoperation, once it has been repaired, a new study will be initiated, covering all the areas usually covered in the completion study, as if this was the first time the carotid artery is closed. This new study is recorded into the Vascular Database as a separate study. The amount of time

required to perform each study is recorded separately by annotating in the space provided in the datasheet the time of the day when the study was initiated and when it was completed. The attending surgeon will proceed with termination of the operation when the intraoperative duplex is normal or shows a minor abnormality as defined by our protocol in the section on background and significance, or re-exploration versus termination if a major defect is present. The patients are divided into three groups: 1) patients with normal duplex, 2) patients with a minor defect on the duplex, and 3) patients with an abnormal finding on the duplex. Any changes in the neurologic exam as noted by the care team is recorded. The patients are followed with the standard post-operative duplex schedule at 6 months, and yearly after that. This is modified following the standard management algorithm as dictated by abnormal findings if any. The endpoints of the study are: 1) a carotid duplex of the operated side that remains stable for one year and does not meet criteria for reoperation, 2) the occurrence of a transient ischemic attack, amaurosis fugax or stroke in the cerebral distribution of the operated side, 3) the occurrence of criteria for reoperation of the operated side, namely, neurologic symptoms in the distribution of the ipsilateral carotid artery associated to a lesion considered to be hemodynamically significant or a possible source of embolic material, and restenosis compatible with 60% or greater diameter reduction, 4) death, 5) two years from the time of the operation elapse. The current standard of care at Walter Reed AMC is for patients to undergo an intraoperative duplex following their CEA. The attending surgeon then chooses to revise the procedure or not based on the duplex findings and his choice of intraoperative neurologic assessment. The vascular surgeons in Walter Reed do not currently have a uniform, agreed upon definition of what would constitute a minor defect. The change in the current standard of care is that a uniform definition is agreed upon, and the attending surgeon is expected to abide by this definition when considering whether to re-explore the carotid or not. This definition is supported by the medical literature. The research is the observation of any immediate and long-term difference in outcome among the three groups of patients.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 2 and the total enrolled to date at WRAMC is 60.

The total enrollment to date has been 60 patients since approval in March 2000. The number of 68 reported on the last APR was in error due to a counting mistake, and should have been 58. There have been no adverse reactions and no patients have withdrawn from the study. There has been no new literature since the last APR that has answered, in a prospective fashion, the questions raised by our study. Study enrollment has been slowed by several episodes of pending deployments by the PI and a decrease in the number of patients undergoing carotid surgery in the last year. Additionally, with the expansion of the endovascular program, several patients who were candidates for this study underwent carotid stenting and were not eligible for study. Though enrollment in the last year has been slow, the PI and Vascular Surgery Service have rededicated efforts to aggressively enroll eligible patients. To date, no significant restenosis has occurred in those patients who had small residual defects that have had a follow-up duplex, and no patient that has been followed-up has suffered any neurologic consequence as a result of a small residual defect.

#### CONCLUSIONS

Thus far, minor defects noted on intraoperative duplex do not appear to increase the risk for restenosis nor have they resulted in an increased number of neurologic events. If this trend continues, minor defects can be ignored and can be safely followed with serial duplex examinations.

## DETAIL SUMMARY SHEET

**TITLE:** Clinical And Pathophysiologic Efficacy Of SEPS The Endoscopic Treatment Of Incompetent Perforating Veins Of The Lower Extremity In Patients With Chronic Venous Insufficiency (CEAP classes 4-6).

**KEYWORDS:** gene expression, skin, venous ulcer

**PRINCIPAL INVESTIGATOR:** David L. Gillespie, LTC MC

**ASSOCIATES:** Bader B. Fileta BS, MT (ASCP), AACC; Aneeta Patel MSc; Audrey S. Chang PhD; Jeffrey Anderson, Marcos Rojkind MD, Ph.D.

**DEPARTMENT:** Surgery

**STATUS:** O

**SERVICE:** Peripheral Vascular Surgery

**INITIAL APPROVAL DATE:** 25 July 2000

### STUDY OBJECTIVE

Determine if the addition of SEPS (subfascial endoscopic perforator surgery) to a treatment regimen including conventional surgery and compression therapy alters patient outcomes. Parameters to be observed during the study include:

- a) rate of ulcer healing
- b) ulcer recurrence
- c) post-operative pain and disability
- d) post-operative wound complications
- e) venous hemodynamics as measured by duplex derived valve closure times and air plethysmography
- f) improved overall quality of life as measured by SF 36. This will be the first study to address these critical questions.

Compare the physical characteristics under confocal microscopy of fibroblasts grown in tissue culture from areas of diseased lower extremity skin to normal skin of the thigh before SEPS and 6 months after SEPS.

Examine the effect of correcting lower extremity venous hypertension on the expression of the matrix metalloproteases MMP-1, MMP-2, MMP-9, MMP-13 and the inhibitor of metalloprotease activity TIMP-1 in fibroblasts grown from areas of diseased lower extremity skin to normal skin of the thigh before SEPS and 6 months after SEPS.

### TECHNICAL APPROACH

In this study skin biopsies obtained from patients undergoing venous surgery. Total RNA and protein isolated are isolated. The RNA is then reverse transcribed using the First Strand cDNA Synthesis Kit (Boehringer Mannheim, Indianapolis, IN) using primers specific for MMP-1, MMP-2, MMP-9, MMP-13 and TIMP-1. RT-PCR product is then separated over 2% agarose gel containing ethidium bromide (0.5 &g/&ml) and visualized by UV irradiation and will be photographed using a Polaroid documentation system.

Western blots are performed using monoclonal mouse anti-human antibodies MMP-1, MMP-2, MMP-9, MMP-13 and TIMP-1 will be used as the primary antibodies (Oncogene Science, Cambridge, MA). Goat anti-mouse horseradish peroxidase coupled antibodies will be used as secondary antibodies. Scanning densitometry is then performed (NIH imager v.1.57) to quantify the amount of these proteins in each sample. Activity of these enzymes is then performed using gel substrate zymography.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Prior work in our lab has demonstrated alterations in matrix metalloprotein expression and activation exists in patients with venous insufficiency when compared to controls. In addition we have found that the activation of these matrix-remodeling proteases varies by location in the leg. Based upon these observations and a review of the literature we propose to not only examine the differences in clinical benefit and physiologic changes but we also propose to use this opportunity to look for changes in dermal fibroblast expression of these matrix metalloproteases. Specifically we are interested in looking at the expression of MMP-1 MMP-2, MMP-9 MMP-13 and TIMP-1 in dermal biopsies of normal skin in the thigh to diseased dermal fibroblasts of the lower leg in patients with chronic venous insufficiency CEAP class 4-6.

More recent data from our lab has shown that the increase in matrix metalloproteinases in the ankle skin of these patients is associated with a corresponding increase in both inhibitors of MMPs namely TIMP-1 and inducers of MMP expression such as the extracellular matrix metalloproteinase inducer CD147/EMMPRIN.

The most major progress that we have made in our laboratory has been our success in growing fibroblasts from skin biopsies of patients with severe chronic venous insufficiency. Thus far we have been successful in placing both normal fibroblast from thigh skin biopsies and abnormal wound skin biopsies from a total of 5 patients into culture. The next phase of our research will be to characterize these cells and then begin to look at the expression of MMP.

The number of subjects enrolled to the study since last APR at WRAMC is 7 and the total enrolled to date at WRAMC is 26.

CONCLUSIONS

We have enrolled 26 patients to date. PCR and Western Blot analysis have been performed on twenty of these patients specimens looking for the expression of CD147/EMMPRIN, MMP-1,8 and TIMP-1. This data is currently undergoing statistical analysis. The 6 other patient's samples have been grown in cell culture in preparation for upcoming experiments.

## DETAIL SUMMARY SHEET

TITLE: Evaluation of Digital Fundus Images as a Diagnostic Method for Surveillance of Diabetic Retinopathy

KEYWORDS: Diabetes mellitus, Eye, Retina, Telemedicine, Vision

PRINCIPAL INVESTIGATOR: Chun, Dal W., CPT MC

ASSOCIATES: Robert M. Bauer, MAJ MC, Thomas P. Ward, COL MC, John Dick, COL MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: Ophthalmology

INITIAL APPROVAL DATE: 14 December 1999

### STUDY OBJECTIVE:

To compare the presence of and extent of diabetic retinopathy determined by examination of digital fundus images with that determined by ophthalmoscopic examination.

### TECHNICAL APPROACH:

Fundus images are obtained from diabetic patients using a nonmydriatic digital fundus camera. The images are transferred from the camera to a viewing station by T1 connection. Images are evaluated for signs of diabetic retinopathy by recognition of presence and extent of physical findings as outlined by the Early Treatment of Diabetic Retinopathy Study and used commonly in clinical practice to determine treatment guidelines. The level of agreement of such findings ascertained by clinical examination is compared statistically with findings from review of the digital images by kappa analysis.

### PRIOR AND CURRENT PROGRESS:

Several recent studies have suggested that evaluation of nonmydriatic fundus photographs provide a cost-effective alternative for screening large numbers of patients for diabetic retinopathy. One objective of the proposed study is to determine if digital imaging of fundus photographs can serve as a consistently reliable method for detection of high-risk diabetic retinopathy, which requires immediate treatment or close surveillance. It is hoped that digital fundus photography could serve as a cost-effective option for screening of retinopathy in a large population of diabetic patients. This technique would also allow an ophthalmologist to examine the eyes of a patient who resides at a distant site promptly and without the need for travel. Such benefits would be extremely useful for the delivery of optimal and cost-effective medical care to soldiers and their families assigned at locations far from a military medical center.

Thirty patients have been enrolled in this study to date. Twenty male subjects and ten female subjects. The average age is 64 years. The number of subjects enrolled to the study since last APR at WRAMC is 0, and the total enrolled to date is 30. WRAMC is the sole site where study is being conducted. No subjects withdrew. An additional seventy patients will be enrolled prior to conclusion of study, anticipated in November 2002.

Three eyes were excluded from the study as a result of having had eye surgery during the past year. The prevalence of diabetic retinopathy (determined by clinical exam) among the study group was 28% and the prevalence of macular edema was 8%. This prevalence is similar to those reported in several studies.

Single nonmydriatic, nonstereoscopic digital fundus images were considered gradable by the interpreter in fifty of the fifty-seven images that were reviewed. Poor image quality correlated with physical findings, limiting view of the fundus in all seven cases, surgical grade cataracts in four cases, miotic pupils in two cases, and a total retinal detachment in the other case.

Adverse Events: None. Benefit to patients: Patients enrolled in this study received comprehensive ophthalmologic examinations including detailed exams of the fundus by a vitreoretinal surgeon or medical retinal

specialist. Patients identified as having diabetic retinopathy or other ophthalmologic disorder were provided with regular follow-up examinations and treatments where indicated. Financial interest: The investigators in this study have no financial interest in any of the equipment used in this study.

CONCLUSIONS:

Preliminary results show that review of a single nonmydriatic, nonstereoscopic digital fundus image can recognize diabetic retinopathy at a level consistent with that of clinical ophthalmoscopic examination. Preliminary results show that review of a single nonmydriatic, nonstereoscopic digital fundus image can recognize diabetic macular edema at a level consistent with that of clinical ophthalmoscopic examination. The initial results of this study suggest that processing and interpreting of digital fundus images may be a valid method for screening diabetic retinopathy using telemedicine techniques. Greater enrollment of subjects is necessary to achieve the desired statistical power that would support these preliminary results. These results are ascertained using a single fundus image. Similar results in level of agreement have been reported with a similar number of subjects using stereoscopic imaging, a proprietary imaging system, and a composite results from a collection of five images of different regions of each fundus that was examined. This report is the only study found in a Medline Search from 1966 to present that attempted to ascertain the validity of using digital fundus images to assess diabetic retinopathy.

In the present study, digital fundus images are collected using a commercially available nonmydriatic camera, and fundus-imaging equipment that is currently used for fluorescein angiography in several military ophthalmology clinics. Such resources would make it practically feasible to implement these techniques for screening diabetic retinopathy in the military ophthalmology setting should it be considered advantageous to use this information for that purpose.

## DETAIL SUMMARY SHEET

TITLE: Expression of Markers of Vascular Proliferation in Human Choroidal Neovascular Membranes

KEYWORDS: neovascularization, retinal degeneration

PRINCIPAL INVESTIGATOR: Prem S. Subramanian MAJ MC

ASSOCIATES: Thomas P. Ward LTC (P) MC

DEPARTMENT: Surgery

SERVICE: Ophthalmology

STATUS: C

INITIAL APPROVAL DATE: 4 April 2000

### STUDY OBJECTIVE

To identify cellular markers of neovascularization by determining the expressive of putative vasogenic and tumourigenic genes in surgically excised choroidal neovascular membranes.

### TECHNICAL APPROACH

Harvesting mRNA from surgical and eye bank specimens. This mRNA then will be used in RT-PCR to determine expression levels of the genes of interest (VEGF, TGF-beta, 67-kd laminin receptor, alpha-beta integrin). The PCR technique has been modified to allow the use of fluorescent-tagged primer sequences that may be used in an automated thermocycler to obtain direct quantitation of amplified products. All analyses are to be performed in the DCI labs.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

It has remained difficult to enroll patients in this study since the advent of a new non-surgical, perhaps more effective, treatment for choroidal neovascularization (CNV). This treatment, photodynamic therapy, has become the most popular method for treating CNV. Submacular surgery is now rarely performed. We have no choice but to terminate the study due to our inability to obtain surgical specimens.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 1, if multi-site study. There have been no adverse events reported.

### CONCLUSIONS

None. Study can be closed.

## DETAIL SUMMARY SHEET

TITLE: A Comparison of Standard Intraoperative Fluoroscopy vs. Fluoroscopy Using FluoroNav Stereotactic System

KEYWORDS:

PRINCIPAL INVESTIGATOR: Polly, David LTC MC  
ASSOCIATES:

DEPARTMENT: Orthopaedic surgery and Rehabilitation  
SERVICE: Orthopaedic Surgery

STATUS: C  
INITIAL APPROVAL DATE: 26 October 1999

### STUDY OBJECTIVE

The primary objective of this study is to determine the amount of x-ray radiation used during the placement of spinal instrumentation with standard intraoperative fluoroscopy vs. fluoroscopy using the FluoroNav Stereotactic system.

### TECHNICAL APPROACH

The investigator will perform the spinal fusion surgery using standard methods as determined by the investigator. The first ten procedures will be performed without the use of the FluoroNav system. The next twenty procedures will be performed with the use of the FluoroNav system. To allow surgeons to become familiar and comfortable with the system, the first ten of the twenty procedures with the FluoroNav will be treated as the learning curve. In the event the FluoroNav system experiences operational difficulty, standard fluoroscopy will be used.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Due to technical challenges in using the image guidance equipment, we have not enrolled any more patients and so not anticipate enrolling any more. Also, because of the substantial clinical experience to date (placement > 500 thoracic pedicle screws) the perception of technical difficulty has changed.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 15. The total number enrolled study-wide is n/a, if multi-site study.

### CONCLUSIONS

FluoroNav could be used to safely place thoracic pedicle screws. There was a significant "learning curve" for learning to use the device. With additional experience in placing screws without the device using only conventional fluoro the PI is no longer interested in the additional effort required to use the Fluoro Nav.



## DETAIL SUMMARY SHEET

TITLE: The Radioscaphoid Interval - A Sensitive Indicator of Early Perilunar Instability

KEYWORDS: Wrist, Instability, Radiographic correlation

PRINCIPAL INVESTIGATOR: Kenneth Taylor, MAJ MC

ASSOCIATES: Philip Belmont CPT MC, Scott Shawen CPT MC, Christopher Litts MAJ MC

DEPARTMENT: Orthopaedics and Rehabilitation

STATUS: O

SERVICE: Orthopedic Surgery

INITIAL APPROVAL DATE: 18 April 2000

### STUDY OBJECTIVE

To establish the diagnostic sensitivity and specificity of the radioscaphoid interval in determining early peripheral carpal instability.

### TECHNICAL APPROACH

Patients presenting to the WRAMC Orthopaedic Hand Surgery clinic with physical examination consistent with carpal instability, and matched controls meeting inclusion/exclusion requirements are being enrolled in this study. Measurement from plain film radiographs, clinical examination data and subsequent inoperative findings are recorded as previously outlined in the DCI-approved protocol. There have been no changes to the methodology of this study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no recent articles in the literature addressing directly or indirectly the concepts tested in our protocol. We have not had any adverse events. There have been no findings made over the course of this study that suggest the methodology needs to be changed. As stated above the methodology has not changed since this protocol was approved.

The number of subjects enrolled to the study since last APR at WRAMC is 7 and the total enrolled to date at WRAMC is 17.

### CONCLUSIONS

Still in the data collection phase. No findings as of yet.

## DETAIL SUMMARY SHEET

TITLE: MOSS-Miami and VertiGraft 2 Open-Label Study # 199901

PRINCIPAL INVESTIGATOR: Polly, David LTC MC

DEPARTMENT: Orthopaedics and Rehabilitation  
SERVICE: Orthopedics SurgerySTATUS: O  
INITIAL APPROVAL DATE: 22 August 2000

**STUDY OBJECTIVE** The VertiGraft2 with the MOSS®-MIAMI® Spinal Fixation System has been approved by the FDA for treatment of spondylolisthesis and it is commercially available. The purpose of this study is to assess the performance of the implant using a transforaminal lumbar interbody infusion (TLIF) procedure and report the outcomes. The basis of comparison for this study is the historical controls from prior surgeries and previous WRAMC experience.

**TECHNICAL APPROACH** Preoperative Evaluation: Within three months prior to the surgical intervention procedure, the study subject must be evaluated using the standard health status survey (SF-36) and the Oswestry Disability Index. All procedures in this protocol are normal standard of care. The research part of this study comes from the data collection information from the SF-36, the Oswestry Disability Index and the Clinical Evaluation sheets. Surgical Procedure: On the date of the surgery, the Operative Case Report Form will be completed to include all relevant and required surgical data. Postoperative Evaluations: The study subject is allowed to ambulate when able to do so without undue discomfort and at the discretion of the Investigator. The study subject will be discharged when afebrile and ambulating comfortably, as soon as deemed appropriate by the Investigator. Radiographic Evaluation: In addition to the radiographic evaluation performed prior to surgery, all subjects will be evaluated postoperatively by radiograph. The films will be evaluated on the basis of the standard for fusion ratings. The criteria for the standards are: a score of 0 = no fusion procedure performed, 1 = obvious Pseudoarthrosis, 2 = Possible Pseudoarthrosis, 3 = Fusion status uncertain, 4 = Probable fusion and 5 = Fusion (included sentinel sign and/or bridging trabecular bone). The radiographic views required include: A-P and lateral views at all time frame points. The flexion and extension views will be done at the twelve-month and the twenty-four month follow-ups. In addition to these radiographic views, a CT scan will be performed at the three-month follow-up. These views are normal standard of care to all patients. There have been no modifications to this study.

**PRIOR AND CURRENT PROGRESS** There have been no amendments or modifications to the study. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 29. One patient voluntarily withdrew. There have been three adverse events. One patient was in a motor vehicle accident at 12 weeks post-op with no significant adverse sequelae present. The second patient had an intra-operative pedicle fracture of her right L5 pedicle. A routine CT was done to verify that the screw placement was still okay. At three weeks post-op, her 100-pound dog jumped on her; her pain worsened. She returned to the clinic for evaluation. Her screw displaced further and she went back to the OR to have the screw removed. This is unrelated to the protocol; it is a sequelae of pedicle screw fixation, which is FDA approved for this indication. The third patient had an adverse event during the 2-level TLIF surgery. On the L5-S1 right side while seating the VertiGraft 2, the lamina separated (split) the graft. The VG2 seemed well positioned, provided structural support as desired, and would have been difficult to remove or alter and therefore was left in place and surgery continued. A bone graft substitute (cancellous chips) was placed into the disc cavity. No untoward effects noted.

**CONCLUSIONS** All patients appear to be healing uneventfully. Many have experienced substantial clinical improvement. There have been no fusion failures to date. A single patient has not experienced significant pain relief.

## DETAIL SUMMARY SHEET

TITLE: The Porous-Coated Anatomic Total Hip Prosthesis, Inserted Without Cement; Results After 15 Years in a Prospective Study

KEYWORDS:

PRINCIPAL INVESTIGATOR: Xenos, John S. LTC MC  
ASSOCIATES:

DEPARTMENT: Orthopaedics and Rehabilitation  
SERVICE: Orthopaedic Surgery

STATUS: C  
APPROVAL DATE: 12 September 2000

### STUDY OBJECTIVE:

To report the minimum 15-year results of a consecutive series of 100 primary uncemented total hip arthroplasties using a first generation design.

### TECHNICAL APPROACH

Clinical information including SF-36 General Health Questionnaire and plane radiographs are obtained on each patient in routine follow-up evaluation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Paper is published.

### CONCLUSIONS

Study has been published in 2003 May Issue of Journal of Bone and Joint.

## DETAIL SUMMARY SHEET

TITLE: Spectro-Temporal Properties of Auditory-Visual Integration for Understanding Spoken Language

KEYWORDS: Speech Recognition, Auditory-Visual, Sensory Integration

PRINCIPAL INVESTIGATOR: Kenneth W. Grant, Ph.D., DAC

ASSOCIATES: Steven Greenberg, Ph.D., International Computer Science Institute, Berkeley, CA

DEPARTMENT: Surgery

STATUS: O

SERVICE: Army Audiology and Speech Center

INITIAL APPROVAL DATE: 30 November 1999

### STUDY OBJECTIVE

To determine the effects of across-modality temporal asynchrony on the recognition of nonsense syllables and sentences. This protocol was amended to test four hearing-impaired subjects on nonsense syllable recognition.

### TECHNICAL APPROACH

Speech sentence materials and nonsense syllables were filtered into two or four narrow spectral slits with at least one octave separation between adjacent slits. In the main condition, the audio signal consisted of two filtered speech bands making up the low and high end of the speech spectrum (i.e., 298-375 Hz and 4762-6000 Hz). The visual channel consisted of a video image of female speaker of American English (head, neck, and shoulders) speaking each of the different speech tokens. The stimuli were presented audiovisually with a range of temporal asynchrony conditions between audio and visual stimulus components (-400 ms – audio leading to 400 ms – video leading) being tested. The subject task was to either press a designated area on a touch screen terminal, write down on paper, and or speak back verbatim what s/he heard. Touch screen responses are stored on computer for later analyses.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The CRDA was amended to include work for a new protocol entitled "Discrimination of Temporal Asynchrony Within and Across Sensory Modalities", submitted to DCI and reviewed by the CIC on 10 September 2002. This protocol is awaiting final approval.

A manuscript was submitted to the Journal of the Acoustical Society of America describing work on within and across channel integration of speech cues for consonant recognition.

The number of subjects enrolled to the study since last APR at WRAMC is 13 and the total enrolled to date at WRAMC is 13. The total number enrolled study-wide is 13, if multi-site study.

### CONCLUSIONS

Spectrally sparse audio comprised of two narrow bands of widely separated speech, or speechreading information, provides modest intelligibility when presented alone in the absence of the other modality. However, this same information can, when combined across modalities, provide good intelligibility (63% average accuracy for sentence materials, 90% for nonsense syllables). When the audio signal leads the video, intelligibility falls off rapidly as a function of modality asynchrony. When the video signal leads the audio, intelligibility is maintained for asynchronies as long as 200 ms. For eight out of nine subjects, the highest intelligibility is associated with conditions in which the video signal leads the audio (often by 80-120 ms). It is believed that this tolerance to video leading conditions, and intolerance to audio leading conditions, is a combination of evolutionary factors (light traveling faster than sound), neural conduction factors (auditory conduction times greater than visual conduction times), and linguistic factors (visual speech information related to place of articulation evolves over a relatively long time window of approximately 200 ms).

## DETAIL SUMMARY SHEET

TITLE: Auditory Supplements of Speech reading

KEYWORDS: Audiovisual Speech Perception, Speech reading, Hearing-Impaired

PRINCIPAL INVESTIGATOR: Grant, Kenneth Ph.D. DAC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: O

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 1 August 2000

### STUDY OBJECTIVE

This is a five-year NIH application describing a research program to further understand the benefits and limitations of auditory-visual speech recognition in normal and hearing-impaired individuals. The proposed studies include examinations of the effects of aging, hearing status, and visual acuity on speech recognition in noise and reverberation.

### TECHNICAL APPROACH

Methods will include identification and discrimination of speech sounds (nonsense syllables, words, and sentences) with and without visual cues (i.e., speech reading). Speech signals will be presented in a variety of background noises and under conditions of room reverberation to simulate typical real-world conditions encountered by normal and hearing-impaired individuals. Special purpose equipment to measure various aspects of static and dynamic visual acuity will be employed to determine if elderly subjects are placed under additional processing demands due to deteriorating peripheral vision, especially for motion detection.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Funding for this NIH grant has not been approved. A revised application has been submitted to the National Institute of Aging (a change in institute). No projects have been initiated on this protocol and no subjects have been enrolled.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

None.

## DETAIL SUMMARY SHEET

TITLE: Mentor Saline Filled Testicular Prosthesis Adjunct Study

KEYWORDS:

PRINCIPAL INVESTIGATOR: COL David G. McLeod MC

DEPARTMENT: Surgery

STATUS: C

SERVICE: Urology

INITIAL APPROVAL DATE: 18 January 2000

### STUDY OBJECTIVE

To provide access to this device while the core study data is submitted and reviewed by the Food and Drug Administration (FDA). Once the Mentor Saline filled testicular Prosthesis is cleared for market via the Pre-market Approval (PMA) process, enrollment of subjects into the Adjunct Study will be halted. This control study will collect tracking information on subjects enrolled into the study and information on the incidence and severity of adverse events.

### TECHNICAL APPROACH

Enrollment is done through patient screening in the Urology Clinic or referred to us from other urology departments in the military. Male military health care beneficiaries age 18 years of age or older who are indicated for testicular prosthesis implantation (in cases of testicular agenesis or following surgical removal of the testis) either unilaterally or bilaterally are enrolled.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The protocol was approved in January 2000. There were 16 patients enrolled in this study at WRAMC and 151 enrolled study-wide. Adverse events have been reported to the HUC in August of 2001 and March of 2002. The protocol is now closed as the FDA has approved the device for use in the U.S. in July 2002.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 16. The total number enrolled study-wide is 151, if multi-site study.

### CONCLUSIONS

The FDA has approved this device for use in the U.S. and it is available through Mentor Corporation for surgical implantation.

## DETAIL SUMMARY SHEET

TITLE: Noninvasive Screening for Coronary Artery Disease Using A Digital Electronic Stethoscope

PRINCIPAL INVESTIGATOR: Popa, Christian MAJ MC

ASSOCIATES: Taylor, Allen LTC MC; Gorman, Patrick LTC MC

DEPARTMENT: Surgery

STATUS: C

SERVICE: Critical Care Medicine

INITIAL APPROVAL DATE: 1 August 2000

STUDY OBJECTIVE Primary objective: To define the relationship between digital electronic stethoscope signals and the presence of angiographic coronary artery disease. Secondary objective: To numerically evaluate the presence of angiographically proven CAD stenosis with the output from the DES.

TECHNICAL APPROACH: Methodology: Sonographers blinded to all clinical data will perform heart sound recordings. Immediately prior to cardiac catheterization a foam acoustic chamber will be placed on the subject's chest using the xyphoid process as a reference mark. The purpose of this device is to standardize sound acquisition with the DES and dampen extraneous sounds. The acoustic chamber contains *nine* recording positions that correspond to the following anatomic locations:  $RSB_1$ ,  $RSB_2$ ,  $RSB_3$ ,  $LSB_1$ ,  $LSB_2$ ,  $LSB_3$ ,  $S_1$ ,  $S_2$ ,  $S_3$ . Once the acoustic chamber has been correctly placed on the subject, the digital electronic stethoscope will be placed at each listening position, the acoustic chamber lid closed, and 20 seconds of sound data collected. Recordings will be made with the subject in a semi-recumbent position at 30 degrees. A simultaneous EKG will be taken for integration into the sonospectrographic recording. It is anticipated that the entire data set acquisition will take approximately 15 minutes per patient. Following data collection, elective coronary angiography will proceed as planned. Data Collection: Following informed consent, a cardiac history will be collected for the purpose of descriptive reporting. Supine blood pressure will be measured using an automated blood pressure cuff. Sonographic data will be collected as described above using the nine designated listening positions of the acoustic chamber with 20-second recordings at each position. Left and right coronary cineangiograms will be obtained at the discretion of the angiographer. Sample Size/Data Analysis: Endpoints: Coronary angiographic data will be analyzed by Dr. Gorman without knowledge of the DES data. The primary variable of interest is the worst angiographic stenosis in a major epicardial coronary artery measured with an automated edge detection system for quantitative coronary angiographic analysis. Signal data from DES will be forwarded to Randy Ford, PhD at SonoMedica for analysis. Signal data are stored as electronic files on Write Once Read Many (WORM) un-re-writable CDROMs that will provide a permanent record of the acoustic data. Copies of these unalterable CDROMs will be coded and provided to WRAMC as a record of the acoustic tests to assure that there is no bias in the correlation of the data comparison between angio and acoustic records. Patient confidentiality will be preserved by labeling each study with an anonymous identifier (study enrollment number). The optimal measurement from DES for correlation with coronary angiography is unknown. Two values will be used: 1) The threshold-presenting signal, and 2) The maximal observed acoustic frequency. Signal data results will be provided to the PI for further analysis as described below. Secondary analysis: Agreement between the two methods (angiography and DES) will be further described using ROC curve analysis. An ROC curve will be constructed for the sensitivity and specificity of the diagnosis of angiographic stenosis by DES.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE There has been no new published literature concerning this technology that would impact this study. Since our last APR 5 August 2002, we have not enrolled additional subjects. We have not heard back from the company regarding a willingness to support additional enrollment, therefore this study will be terminated. The number of subjects enrolled to the study since last APR at WRAMC is 56 and the total enrolled to date at WRAMC is 56.

CONCLUSIONS There are no conclusions to report. The study is terminated due to insufficient enrollment and manufacturer support.

## DETAIL SUMMARY SHEET

TITLE: Aberrant T Cell Receptors in Systemic Lupus Erythematosus

PRINCIPAL INVESTIGATOR: Gregory J. Dennis, COL, MC

ASSOCIATES: William N. Fishbein, MD, Ph.D.

DEPARTMENT: Medicine

STATUS: T

SERVICE: Rheumatology

INITIAL APPROVAL DATE: 7 March 2000

### STUDY OBJECTIVE

Compare the percentage of aberrant T cell receptors in patients with systemic lupus erythematosus to that of rheumatoid arthritis.

### TECHNICAL APPROACH

Using the chromosome 7 inversion assay blood samples of patients with these diseases will be analyzed for the presence of V $\gamma$ -J $\beta$ 1 hybrid T-cell receptors and quantified as the number of inversions per ug DNA. Samples have been further analyzed using a non-radioactive PCR and Southern blot followed by chemiluminescent detection. The latter probe will allow an important comparison of the technique in this patient population.

### PRIOR AND CURRENT PROGRESS

Number of subjects enrolled to study since last APR at WRAMC is 0. Total enrolled to date at WRAMC is 54.

### CONCLUSIONS

Study terminated due to failure to submit Annual Progress Report.



## DETAIL SUMMARY SHEET

TITLE: GOG 178 Phase III Randomized Trial of 12 Months vs. 3 Months of Paclitaxel in Patients with Advanced Ovarian, Fallopian Tube or Primary Peritoneal Cancer Who Attain a Clinically Defined Complete Response (CR) Following Platinum/Paclitaxel-Based Chemotherapy

KEYWORDS:

PRINCIPAL INVESTIGATOR: G. Scott Rose, LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 25 July 2000

STUDY OBJECTIVE:

To assess whether the continuation of paclitaxel, a cycle specific antineoplastic agent, for 12 months following the attainment of a clinically-defined complete response (CR) to initial platinum (carboplatinum or cisplatin)/paclitaxel-based chemotherapy can significantly increase progression-free survival and overall survival when compared to a 3-month continuation in women with advanced ovarian, fallopian tube or primary peritoneal cancer. To assess the toxicities associated with prolonged paclitaxel.

TECHNICAL APPROACH

This is a Phase III study. Patients on this study will be receiving paclitaxel either for a 12-month cycle (12 courses) or over a 3-month cycle (3 courses). Patients are followed for progression-free survival and overall survival and toxicities.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The Southwest Oncology Group Data and Safety Monitoring Committee (DSMC) reviewed a protocol-mandated interim-analysis on 10/25/01 and recommended closing the study to accrual due to a positive result indicating a beneficial effect on progression-free survival associated with the 12-month consolidation treatment.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 3. The total number enrolled study-wide is 152, if multi-site study.

CONCLUSIONS

Consolidation therapy of advanced ovarian cancer with 12 monthly cycles of single agent paclitaxel results in an improvement in progression-free survival (median 28 months) compared to 3 monthly cycles of single agents paclitaxel (median 21 months) (p=0.023).

Data on overall survival remain immature.

## DETAIL SUMMARY SHEET

TITLE: GOG 9901 - Comparison of Quality of Life for Ovarian Germ Cell Cancer Survivors

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott, LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: C  
INITIAL APPROVAL DATE: 15 August 2000

### STUDY OBJECTIVE

To compare germ cell tumor survivors with a matched control group of well females on the quality of life variables of health status and sexual functioning. Psychological and emotional well-being and social functioning will be compared as secondary end points.

### TECHNICAL APPROACH

Patients with early and advanced ovarian germ cell tumors who have previously been enrolled on GOG protocols 45, 78, 90, and 116. Patients and control individuals will complete a self-administered questionnaire. They will also be administered a variety of instruments that will assess physical and sexual functioning, social networks, and psychological functioning. A detailed statistical analysis will be done to compare patients and controls for these variables.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This is the first APR for this study at WRAMC. There have been a couple of publications reporting data for this study. The objectives of this investigation have not been fulfilled by prior studies.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 108, if multi-site study.

Ref: Jan 03 GOG Statistical Report

### CONCLUSIONS

Too early. Study closed with no patient enrollment from WRAMC.

## DETAIL SUMMARY SHEET

TITLE: GOG 175 - A Randomized Phase III Trial of IV Carboplatin (AUC 6) and Paclitaxel 175 mg/m<sup>2</sup> Q 21 Days x 3 Courses Plus Low Dose Paclitaxel 40 mg/m<sup>2</sup>/wk vs. IV Carboplatin (AUC 6) and Paclitaxel 175 mg/m<sup>2</sup> q 21 Days x 3 Courses Plus Observation in Patients with Early Stage Ovarian Carcinoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC

ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology

STATUS: O

SERVICE: Gynecologic Oncology Group

INITIAL APPROVAL DATE: 15 August 2000

STUDY OBJECTIVE

To compare the progression-free interval and overall survival in the two treatment arms. To assess the frequency and severity of toxicities due to the continued low dose paclitaxel regimen. To investigate markers of angiogenesis and metastasis as prognostic indicators for early stage epithelial ovarian cancer.

TECHNICAL APPROACH

All patients must have a histopathologic diagnosis of epithelial ovarian cancer. Patients with sufficient tumor tissue must have tissue specimen(s) sent to the GOG Tissue Bank.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 354, if multi-site study. Grade 4 toxicities include 2 WBC, 2 platelets, 104 granulocytes, 1 allergy, 1 cardiovascular, 3 gastrointestinal, and 2 neurologic.

Ref: Jan 03 GOG Statistical Report

CONCLUSIONS:

Too early.

## DETAIL SUMMARY SHEET

TITLE: GOG 171 Expression of the MN Protein in Atypical Glandular Cells of Undetermined Significance (AGUS or AGCUS) as Potential Diagnostic Biomarker of Cervical Dysplasia/Neoplasia

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 26 September 2000  
NEW ANNIVERSARY MONTH: 26 August

STUDY OBJECTIVE

To evaluate the utility of a novel tumor-associated antigen termed "MN" as a potential diagnostic biomarker for cervical glandular and/or squamous neoplasia in patients with cytologic diagnosis of atypical glandular cells of undetermined significance (AGUS). To measure the frequency and type of cervical pathology associated with AGUS diagnosis.

TECHNICAL APPROACH

Patients with cytologic diagnosis of AGUS in whom complete histological examination of cervix (cone or LEEP biopsy) is planned will be eligible for this protocol.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's last review, there have been no publications reporting data from studies with similar study design in the literature. The number of subjects enrolled to the study since last APR at WRAMC is 2 and the total enrolled to date at WRAMC is 26. The total number enrolled study-wide is 438, if multi-site study.

CONCLUSIONS:

Too early.

## DETAIL SUMMARY SHEET

TITLE: A Trial of Vitamin B Complex for the Treatment of Chemotherapy Induced Peripheral Neuropathy

KEYWORDS: Vitamin B Complex, Neuropathy

PRINCIPAL INVESTIGATOR: LT Jay Allard, MC USN

ASSOCIATES: Rogers, Stacey J. LCDR MC; Aylesworth, Cheryl, MD; Giroux, Donna, RN, BSN; Petrov, Jean, RN, MS

DEPARTMENT: Obstetrics & Gynecology  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 18 April 2000

### STUDY OBJECTIVES:

To determine if vitamin B complex is effective in the treatment of chemotherapy induced neuropathy and to determine the side-effects of such treatment.

### TECHNICAL APPROACH

There have been no modifications since the protocol was approved. Subjects receiving chemotherapy with a Taxol-containing regimen who develop peripheral neuropathy are given vitamin B complex twice a day for 6 weeks. Subjects are queried at baseline (prior to starting the vitamin B complex), weekly during the study, and at the conclusion of the study regarding their neurologic symptoms and any changes that occur during the course of the vitamin treatment. A brief neurologic examination is performed at baseline and at the completion of the six weeks of treatment. Based on the questionnaires and neurologic examinations, grades of peripheral neuropathy are assigned. Response is defined as an improvement in peripheral neuropathy by at least one grade. After 25 subjects who can be evaluated have been accrued, statistical analysis will be performed to determine if further study is warranted.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no modifications since the protocol was approved. This is the third APR for this study. There have been a total of 19 patients enrolled to date. There has been one subject withdrawn from the study prior to completion due to facial flushing associated with the vitamin B complex. The flushing resolved upon discontinuation of the complex. This adverse event was not serious. As noted in the consent form, facial flushing is usually seen at higher dosages than given in this study. All subjects have reported the expected color change and/or odor in their urine.

Summary of findings to date: Of the 19 subjects enrolled, 1 subject was withdrawn prior to the completion of 6 weeks of vitamin B complex treatment. Of the 18 remaining patients, six have responded with a decrease in the grade of their neuropathy noted and 12 have not responded to treatment with the complex. The number of subjects enrolled to the study since last APR at WRAMC is 8.

### CONCLUSIONS

Based on the number of responses to date, and the parameters set forth in the data analysis portion of the protocol, continuation of the study is warranted. If found to significantly decrease the severity of chemotherapy induced peripheral neuropathy, this treatment could significantly impact the quality of life of these patients and potentially allow for dose escalation of chemotherapeutic agents. Further study via randomized trial would be recommended to compare the vitamin B complex to placebo, as well to ensure the vitamin treatment does not adversely affect patient survival (currently unknown). Patient accrual is planned until 25 evaluable patients are entered or seven have been found to respond to treatment with the vitamin B complex. Based upon our analysis, this will allow us to detect a true response rate of at least 30% with a power of 0.93.

## DETAIL SUMMARY SHEET

TITLE: A Prospective, Randomized, Double Blind, Placebo Controlled Study of Oral Misoprostol Prior to Operative Hysteroscopy

PRINCIPAL INVESTIGATOR: McKeeby, Jeffery CDR  
ASSOCIATES: Preen, Amy CPT MC

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Reproductive Endocrinology

STATUS: O  
INITIAL APPROVAL DATE: 27 June 2000

### STUDY OBJECTIVE

Null hypothesis: Oral misoprostol prior to hysteroscopy will not enhance cervical dilation or decrease operating time. We will investigate the time needed for cervical dilation, time needed for hysteroscopy and the ease at which hysteroscopy is performed with preoperative administration of misoprostol. If oral misoprostol is effective in softening the uterine cervix, we expect that operative time; complication rate and patient post-operative discomfort will all be reduced. Primarily, we plan to measure length of dilation, length of surgery, and the first noted cervical dilator with resistance. Secondly, we plan to subjectively assess ease of procedure and the patient's symptoms prior to surgery and post-operative pain. We will assess the incidence of complication such as uterine perforation.

### TECHNICAL APPROACH

1. Patients will have been already been scheduled for an indicated operative hysteroscopy at Walter Reed Army Medical Center will be advised of the study. All patients undergoing operative hysteroscopy have urine HCG the day of surgery to assure the patient is not pregnant.
2. At their routine scheduled pre-operative visit patients will be counseled as to the risks, benefits, and alternatives and then sign the consent to participate in the study. Once they have signed the consent they will be given an opaque coded sealed envelope that will contain a misoprostol 400-microgram capsule (an orally approved drug, provided by the Walter Reed Army Medical Center pharmacy) or placebo. Factors (menopausal status, parity, and use of estrogen replacement therapy) that may affect the outcome measure (i.e. time needed for cervical dilation) will be determined for stratification. Patients within each stratum will be randomized to either misoprostol or placebo with equal number. Randomization will be by assignment of a random number generated by the DCI random number generator for each stratified group. The pharmacy will have a copy of the randomization scheme. However, the pharmacist will not have access to it. Patients will be given a pre-questionnaire to fill out the time and date the capsule was taken and any side effect experienced.
3. They will take the capsule the night prior to surgery, approximately 12 hours prior to the procedure. Twelve hours will be determined from the planned operation scheduled time. Patients will be asked to record the time the capsule was taken.
4. When they arrive for surgery approximately 12 hours later they will finish the pre-questionnaire regarding any noted discomforts or symptoms they experienced after taking the capsule. The time the capsule was taken should have already been recorded. This questionnaire will be completely filled out prior to the procedure and collected by the operating surgeon.

5. The surgeon will fill out a questionnaire to include basic information about the surgery (secondary outcomes): the procedure performed (for example: myomectomy, polypectomy, septum resection; adhesiolysis), media used (sorbitol, saline, hyskon, mannitol or CO2), and the total media deficit. The questionnaire will also include primary endpoints: time at start of dilation, time at finish of dilation (largest dilator needed to place operative hysteroscope), first cervical dilator with noted resistance, start time, and finish time of hysteroscopy. Secondary end-points will also be recorded: ease of procedure (visual analogue scale) and any complications that occurred.
6. The day after the procedure the patient will be called by a department secretary to remind them to fill out the post-procedure questionnaire. The patient will be asked to rate post-operative discomfort on a visual analogue scale along with any side effects they have felt regarding the medicine and the procedure. They will record these on a post-questionnaire given to them prior to discharge from the hospital. A stamped/addressed envelope will be supplied for patients to mail it back to the department.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

After evaluating 46 patients in each arm of the study, we found no benefit to oral misoprostol. We have not enrolled additional patients for this protocol largely due to difficulty in obtaining the placebo misoprostol. We are preparing a manuscript for publication.

One publication recently showed a benefit to oral misoprostol: Am J Obstet Gynecol 2002 May;186(5):876-9

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 47.

#### CONCLUSIONS

No new patients have been enrolled since the last APR. After evaluating 46 patients we have found no benefit for oral misoprostol. We are preparing a manuscript of this finding for publication.

## DETAIL SUMMARY SHEET

TITLE: Characterization of Peritoneal Fluid in Differentiating Benign from Malignant Adnexal Masses

KEYWORDS:

PRINCIPAL INVESTIGATOR: McBroom, John MAJ MC

ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology

STATUS: C

SERVICE: Gynecologic Oncology

INITIAL APPROVAL DATE: 05 July 2000

### STUDY OBJECTIVE

To determine if peritoneal fluid LDH, cholesterol, or interleukin-6 levels can discriminate between benign and malignant adnexal masses. We will also compare the serum to peritoneal fluid ratios to determine if this augments the ability to discriminate.

To determine if these chemistry values are significantly different between women with an adnexal mass and those without an adnexal mass.

### TECHNICAL APPROACH

This research study involves patients who are scheduled to undergo surgery in the gynecology department. They will evaluate the fluid in the patient's peritoneal cavity and their blood for chemical markers. These markers may have the ability to determine if a patient with a mass has cancer or not. If they are undergoing gynecologic surgery and do not have a mass the patients participation is needed in order to compare their values to those women with a mass.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review a year ago, there have been no publications reported.

The number of subjects enrolled to the study since last APR at WRAMC is 5 and the total enrolled to date at WRAMC is 20.

### CONCLUSIONS

Statistically significant difference found between benign and malignant group in peritoneal IL-6 value.



## DETAIL SUMMARY SHEET

TITLE: Feasibility, Accuracy and Efficiency of an Internet Based Tele-Nuclear Consultation System for the Military, Phase I: Phantom Studies

PRINCIPAL INVESTIGATOR: Stack, Aaron L. MAJ MC

ASSOCIATES: B. Cannon, RN; E. Quang, Ph.D.; LTC Poropatich; COL L. Nagorski; MAJ C. Jimenez

DEPARTMENT: Radiology

STATUS: O

SERVICE: Nuclear Medicine

INITIAL APPROVAL DATE: 12 October 1999

### STUDY OBJECTIVE

1. To determine the feasibility of an Internet based Tele-Nuclear consultation system between Walter Reed Army Medical Center and Fort Knox Department of Radiology. Feasibility is defined as the technical ability to perform this transmission and review using existing technology. Efficiency is defined as the speed of transmission and time of evaluation using the system.
2. To examine the concordance in the image quality between native phantom studies vs. those reviewed using the Internet based Tele-Nuclear system.
3. To examine the concordance in the diagnosis between native phantom studies vs. those reviewed using the Internet based Tele-Nuclear system.

### TECHNICAL APPROACH

This is a prospective concordance trial using similar data from two locations. The image phantoms will be filled with appropriate radiopharmaceutical agents, and images will be acquired at Fort Knox using the protocols sent out by the ACNP. Two nuclear medicine physicians at WRAMC will score these studies independently. Rater 1 will review the six phantoms at Fort Knox, while rater 2 will review the data acquired from the six phantoms via the Internet based system at WRAMC. After a one-month delay to insure reader blinding, rater 2 will then review the phantoms at Fort Knox while rater 1 reviews the phantoms at WRAMC. A third nuclear medicine physician at Rodrigues Army Health Clinic, Puerto Rico will provide an independent reading of only the transmitted images from Fort Knox for comparison. By having a third reader, we can evaluate the concordance between two readers blinded to the transmitted study. These sets of data will be evaluated for concordance.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

During the past year, the main focus was on determining exactly what had been done in the year's prior. It appears that the system was installed by Sudbury, Inc., and tested once. One image was sent from Fort Knox to WRAMC. PI has not been able to locate this image. The software used at WRAMC to view the sent images, (Open PACS), has expired and was deleted from the system during an upgrade of operating systems to Windows 2000. WRAMC has paid Sudbury for the contract and Sudbury feels they have met their initial obligation. There are only a few thousand dollars left in the initial budget for this project. PI's goal for the coming months is to evaluate the viability of this project, as it has passed through two other PIs previously. In order to complete the project, PI needs to get current software installed on PCs at WRAMC, and WRAMC needs to give Sudbury access to our computers at WRAMC, which is a security problem and will cost additional money. Unfortunately, this project was basically ignored for about a year and a half prior, and PI is unsure at this point if it is still a viable project. PI asks for another year to investigate the options. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS:

The next year will determine viability and need of this project, as current technology has proven tele-radiology to be an accurate means of off-site image interpretation. PI also needs to verify that the contract obligations of the vendor, Sudbury, Inc., have been met.

## DETAIL SUMMARY SHEET

TITLE: Role of Focal Matrix Metalloproteinases in Differentiated Thyroid Cancer

KEYWORDS: metalloproteinase, thyroid, cancer

PRINCIPAL INVESTIGATOR: Francis, Gary COL MC  
ASSOCIATES:

DEPARTMENT: Pediatrics  
SERVICE: Pediatric Endocrinology

STATUS: C  
INITIAL APPROVAL DATE: 30 November 1999

### STUDY OBJECTIVE:

This study is designed to determine if the expression of matrix metalloproteinases is increased in a group of archived paraffin-embedded thyroid tissue blocks when compared to a similar group of archived benign thyroid lesions. If so, this would provide evidence that metalloproteinases are important in thyroid cancer and would offer a novel therapeutic window of inhibitors of metalloproteinases for this disease.

### TECHNICAL APPROACH:

Archived thyroid tissues are deparaffinized and stained by immunohistochemistry for matrix metalloproteinase expression. The intensity of staining is graded by two independent examiners and then compared to the rate of recurrence, tumor size, and presence of metastasis.

### PRIOR AND CURRENT PROGRESS:

Archived samples had been obtained under Work Unit # 6414. No patients were contacted or examined.

### CONCLUSIONS:

Archived tissues have been stained and data submitted for publication. (32 papillary thyroid cancers, 7 follicular thyroid cancers, and 12 benign lesions.)

## DETAIL SUMMARY SHEET

TITLE: POG 9900 - ALinC 17 Classification Protocol – A Pediatric Oncology Group Non-Therapeutic Study

KEYWORDS: lymphoblastic, leukemia, classification

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Crouch, Gary LtCol MC; Merino, Margret MAJ MC; Reddoch, Shirley MD

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 15 August 2000

### STUDY OBJECTIVE

(1) To provide the clinical and laboratory data necessary for placing each patient with Acute Lymphoblastic Leukemia (ALL) onto the proper therapeutic trial. (2) To provide an administrative base to capture classification data for correlative studies in ALL treatment protocols and series of historical protocols.

### TECHNICAL APPROACH

This is a non-therapeutic laboratory classification study for subjects with newly diagnosed ALL < 21 years of age at the time of diagnosis. Through local and reference laboratories each subject will have there leukemic cells biologically sub classified at the time of diagnosis using a variety of laboratory methods. This information will be used to place each subject onto the proper therapeutic trial.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study opened to accrual on 12/13/1999. As of 12 June 2003, group wide accrual is 2794. WRAMC has seven registrants, one since the last APR. Since this a non-therapeutic study, there is no toxicity data to report. Detailed reference laboratory reports can be found in the POG 9900 Spring 2003 Study Progress Report.

C. O. G. amended this study twice since the last APR – COG amendments 3 and 4; both were approved by WRAMC's HUC. Benefit to subjects is proper identification of leukemia subtype to determine appropriate therapy.

The number of subjects enrolled to the study since last APR at WRAMC is 1 and the total enrolled to date at WRAMC is 7. The total number enrolled study-wide is 2794, multi-site, as of 12 June 2003.

### CONCLUSIONS

Study should remain open.

## DETAIL SUMMARY SHEET

TITLE: POG 9907 - ALinC 17 Cytogenetics Protocol – A Pediatric Oncology Group Non-Therapeutic Study

KEYWORDS: cytogenetics; lymphoblastic; leukemia

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Crouch, Gary LtCol MC; Merino, Margret MAJ MC; Reddoch, Shirley MD

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 15 August 2000

### STUDY OBJECTIVE

Assess the feasibility of obtaining high quality decentralized cytogenetic karyotyping in POG. To continue the POG tradition of having well cytogenetically characterized patients for use in correlative and descriptive cross-protocol studies in POG and in international collaborative analyses.

### TECHNICAL APPROACH

Children < 21 years of age with newly diagnose acute lymphoblastic leukemia (ALL) will have their leukemia cells karyotyped at a COG approved cytogenetics laboratory. This information will be compiled and stored in a secure database for use in correlative and descriptive studies of this patient population. In addition, the cytogenetics data, if informative, will be taken into account by the UNM Molecular Reference Laboratory in reporting the DI (including hypodiploidy), FISH 4&10, and molecular detection results for the E2A/PBX-1, t (1;19); the BCR/ABL, (9;22); and MLL (11q23) rearrangements. The cytogenetics data will be considered in any case in which the DNA index, FISH 4&10, or molecular detection results are not straightforward.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study opened to accrual 13 Dec 1999. Group-wide accrual as of 12 June 2003 is 2067. WRAMC accrual is at five, one since the last APR. Data evaluation continues to show impressive results in the concordance of karyotype results with the molecular immunophenotypic results in studies performed at the New Mexico and Hopkins reference laboratories. [COG 9907 Study Progress Report, Spring 2003]

Benefit to subjects is the accurate prediction of the best treatment plan.

The number of subjects enrolled to the study since last APR at WRAMC is 1 and the total enrolled to date at WRAMC is 5. The total number enrolled study-wide is 2067 as of 12 June 2003, multi-site study.

### CONCLUSIONS

Study should remain open.

## DETAIL SUMMARY SHEET

**TITLE:** A Randomized Placebo-Controlled Trial of Sertraline for Neurobehavioral Sequelae of Traumatic Brain Injury

**KEYWORDS:** Traumatic Brain Injury, Head Injury, SSRI

**PRINCIPAL INVESTIGATOR:** Deborah L. Warden, M.D.

**ASSOCIATES:** James Ecklund, M.D., Maria E. Graves, RN, COL Bahman Jabbari MC, Elisabeth Moy-Martin, RNC, M.A., Molly Sparling, B.A., Laurie Ryan, Ph.D., Joan Walter, PA

**DEPARTMENT:** Neurology  
**SERVICE:**

**STATUS:** O  
**INITIAL APPROVAL DATE:** 21 March 2000

### STUDY OBJECTIVE

- a. To investigate the efficacy of Sertraline, a selective serotonin reuptake inhibitor (SSRI), in treating neurobehavioral sequelae of irritability, depression, frustration, anxiety and other post-concussive symptoms following traumatic brain injury (TBI).
- b. To explore possible relationships between anosmia (deficits in smell) and irritability/aggression.

### TECHNICAL APPROACH

As the standard of care for patients with traumatic brain injury (TBI) at Walter Reed, patients receive a multidisciplinary evaluation consisting of neurology exam, neuropsychology, psychiatry, psychosocial, EEG, MRI, phlebotomy, and family interview. Research tests include the smell test, evoked potentials, drawing and storing of the blood sample, and some questionnaires related to the subject's medication response. Blood samples (about two tablespoons) are kept at the DVHIP labeled with the patient's study number for possible future use in studies to understand better aspects of recovery from head injury. Blood samples are used in studies of genetic markers potentially related to outcome from TBI. Participants have the option of not consenting to the genetic analyses while still participating in the rest of the protocol. After signing the volunteer informed consent, patients will be randomized into an active drug or placebo group. Patients receive an increasing dose of Sertraline or placebo starting at 50mg (1 pill) and increasing to a dose of 200 mg (four pills) of Sertraline. Dose adjustment is considered every three weeks and is based on scores on the Clinical Global Improvement Scale. Family members or a close friend of the subject are asked to complete some questionnaires after giving informed consent for their participation. The medication phase lasts twelve weeks. Patients receive standard TBI care during this period that may include a period of Convalescent Leave Home (CVL) followed by a gradual return to duty. All patients are contacted weekly during the medication phase to assess general condition, current symptoms, and assessment of compliance. If patients require a clinical medical appointment during the twelve weeks, patients are seen at WRAMC if possible. If not possible, study personnel are available to speak with the patient's clinician at a local medical facility. Patients return to WRAMC at twelve weeks for a follow-up evaluation of their symptoms, or are contacted by phone if unable to return to WRAMC for their twelve-week evaluation. Sertraline blood levels are obtained at twelve weeks as a measure of compliance and as a potential correlate to symptom amelioration. After the twelve-week evaluation, patients are tapered off Sertraline or placebo over two weeks. If subjects have recurrent symptoms following the twelve-week evaluation that are distressing to them, or believe they need medication to keep their symptoms from recurring, pharmacological and nonpharmacologic treatments are discussed with them. Patients are offered appropriate treatment, including Sertraline, if medically indicated. The blind is not yet broken, that is, patients are not able to learn if they were being treated with placebo or Sertraline. Subjects are contacted by phone or seen at 3, 6, 9, and 12 months following their twelve-week follow-up evaluation for an assessment of their symptoms and general level of functioning. If patients are in the area, these follow-up evaluations are done in person.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Two addenda have been approved by DCI and implemented this year. The first involved an update to the investigators/collaborators, the addition of collaborative centers, clarification of research tests administered during the protocol, updates to the inclusion/exclusion criteria, and extension of the study time line to Winter of 2005. The second addendum was for use of an advertisement to aid in recruiting potential study participants. On 7 November 2002, we requested a change of Medical Monitor.

We currently have enrolled fifteen patients at WRAMC. Three participants have been enrolled at San Diego Naval Medical Center, and two at Wilford Hall US Air Force Base. One unexpected adverse event was reported in October 2002. It is unclear if this adverse event is related to the protocol.

The number of subjects enrolled to the study since last APR at WRAMC is 5 and the total enrolled to date at WRAMC is 15. The total number enrolled study-wide is 20. A recent literature search completed 26 December 2002 revealed no new research directly relating to this protocol.

CONCLUSIONS

Subject enrollment is currently underway and we feel that the protocol is running smoothly. There have been no serious adverse events related to the protocol to date.

## DETAIL SUMMARY SHEET

TITLE: Effectiveness of Botulinum Toxin Type-A in the Treatment of Migraine Headache - A Randomized Controlled Trial.

KEYWORDS: Migraine, headache, Botox

PRINCIPAL INVESTIGATOR: Labutta, Robert, COL, MC;

ASSOCIATES: Jabbari, Bahman, COL, MC; Murray, Evan, MAJ, MC; Kudelko, Kenneth, CPT, MC; Petit, Cynthia MSN, CRNP

DEPARTMENT: Neurology

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 26 September 2000

STUDY OBJECTIVE:

We hypothesize that patients who receive injections of Botulinum toxin type A (BOTOX; BTX-A) into selected pericranial muscles will experience a significant reduction in the frequency of headaches and/or the average severity of the headache attacks. We intend to evaluate the efficacy of BTX-A as a prophylactic therapy for migraine headache.

Technical Approach: This study is a prospective, randomized, double blind, placebo-controlled trial that compares the efficacy of BTX-A injections with placebo in migraine headache prevention. Patients will record the frequency and intensity of headaches in a daily diary for a 1-month baseline period and for 6 months after they receive a single treatment or placebo dose to selected pericranial muscles. The primary outcome measure is the average frequency of headache days measured during 30-day blocks for six months. The secondary outcome measures are the severity of attacks using a visual analog scale (VAS) from 0-10 (0=no headache pain; 10 =most severe headache pain experienced) and the Migraine Specific Quality of Life Questionnaire (MSQ). No modifications were made to the protocol.

Scientific Rationale: (BTX-A) is a purified derivative of the exotoxin produced by the bacteria *Clostridium botulinum*. The neurotoxin attaches to, and crosses, the presynaptic plasma membrane and cleaves SNAP-25, a 25kD protein that is critical for the release of acetylcholine from the synaptic vesicles situated within nerve endings. The agent inhibits the release of vesicle-bound acetylcholine, thereby blocking neuromuscular transmission and causing temporary muscle paralysis. BTX is known to have a blocking action on the parasympathetic nervous system that may also inhibit the release of a number of neurotransmitters and neuropeptides other than acetylcholine, including glutamate, norepinephrine, dopamine, substance P, and calcitonin gene-related peptide. The ability of BTX-A to inhibit the release of acetylcholine at the neuromuscular junction and to reduce muscle tone is well established; however, its mechanism of action in the prevention of headache is less clear.

In patients with tension-type headaches, the central modulation of pain perception may be altered and results in a cycle of hypersensitivity that begins at the peripheral muscle. Botulinum toxin affects intrafusal muscle spindles involved in a sensory feedback loop to the spine and central nervous system and may indirectly alter sensory perception and sensitization. Results of several recent clinical trials demonstrate that BTX-A is an effective prophylactic agent in the management of migraine. In an open label study, 39/77 (51%) of patients treated with BTX-A had a complete response with mean duration of benefit of 4.1 months. Individuals with low baseline headache frequency were more likely to report a complete response than individuals with high baseline frequency; however, the proportion of patients who noted improvement (complete or partial response) did not depend on the baseline severity or frequency of headache. These results were later confirmed in a double blind, placebo-controlled trial. Previous headache studies used doses of BTX-A that ranged from 25 U to 200 U. Schulte-Mattler et al. used a total dose of 200 U of BTX-A that was divided equally among the frontal, temporal, occipital and sternocleidomastoid muscles for the treatment of tension-type headache. Only one of eight patients had a treatment-related adverse effect, a transient sensation of slight muscle weakness in the posterior neck. Freund, et al. injected a total dose of 100 units of BTX-A into various painful trigger

points along the cervical musculature (splenius capitis, rectus capitis, upper trapezius, semispinalis). None of the 14 patients experienced treatment-related adverse effects at four weeks post-injection.

In a recent multicenter, randomized, placebo-controlled trial that assessed the safety and efficacy of BTX-A for the prevention of migraine, patients received either placebo or a total of 25 U or 75 U of BTX-A, which were divided into bilateral injections into frontalis, temporalis, and corrugator muscles. During a one-month baseline period and for three months following injection, patients kept daily diaries in which they recorded migraine frequency, migraine severity, and the occurrence of migraine-associated symptoms. The primary outcome measure in this trial was the frequency of headache as reported by patients in a headache diary. Both doses of BTX-A are significantly superior to placebo in decreasing the number and severity of migraine attacks per month. In addition, patients receiving the BTX-A use less acute migraine medications and experience less migraine-associated vomiting than individuals who received the placebo. The therapeutic index of the 25-unit dose is superior to that of the 75-unit dose. The larger dose is more likely to cause transient paralysis of the levator palpebrae superioris and is associated with a higher incidence of transient ptosis and diplopia. The only BTX-A -associated adverse effects noted in this trial were two cases of transient diplopia and 11 cases of injection site tenderness.

Another double blind, placebo-controlled study demonstrated that BTX-A could reduce the pain intensity of migraine attacks; however, in this trial, BTX-A therapy did not result in a significant reduction in the frequency or duration of migraine attacks. In this trial, patients with IHS-defined migraine were randomized to one of the following injection groups: Group I--BTX-A to the frontal and temporal regions; Group II--BTX-A to the frontal region, placebo to the temporal region; Group III--BTX-A to the temporal region, placebo to the frontal region; and Group 4--Placebo to the frontal and temporal regions. Follow-up data were collected at 2- 4- 8-12-, and 16-week post injection visits from patient diaries that contained the following information: occurrence of migraines, start/stop times of migraines, severity of migraines, migraine associated symptoms, and use of acute migraine medication. Primary outcome measures were frequency, duration, and pain intensity compared with baseline. Group I vs. Group IV at week 12 was defined as the key comparison. Group I maximum pain decrease was significantly greater than for Group IV. Groups I and II experienced greater decreases in migraine duration than Groups III and IV; however, these differences were not significant. There were no discernible differences by treatment group in decrease of migraine frequency, vomiting, or number of migraine day. The investigators concluded that there was a definite trend for BTX-A superiority in reduction of migraine frequency and duration; however, the study lacked adequate power to demonstrate that BTX-A was significantly superior to placebo.

In addition, the results of a recent retrospective study revealed that BTX-A is an effective prophylactic therapy for migraine. The primary outcome measure of this study was relief--defined (by patients) as a reduction in the frequency and our severity of headache attacks. Twenty-three patients had relief that lasted from two to six months. The improvement ranged from a complete elimination of the headaches to a 50% reduction in severity (with unchanged frequency). Four individuals noted no change in the frequency/severity of their attacks. Adverse effects noted in this review include headache immediately after the injection (one patient) and nausea in another individual.

BTX-A has also been effective in the acute treatment for migraine. The agent produced a complete response (i.e., elimination of all headache symptoms) in seven of 10 patients within one to two hours after treatment. In addition, a case of status migraine has responded to BTX treatment. This patients' migraine was refractory to usually effective medications and was treated with 25 U of BOTOX at an acupuncture point for migraine. The patient experienced relief within one hour following injection of the toxin and had no further headaches for two months. (The individual's usual attack frequency ranged from 2-4 attacks per month.) These numerous trials demonstrate that BTX-A is an effective prophylactic therapy for migraine. Additional studies are required to determine the optimal dosage regimen of the agent and to identify the subpopulation of patients with migraine who are most likely to have an excellent response to BOTOX therapy.

**BTX-A Pharmacokinetics:** When BOTOX is administered as an IM injection at recommended doses, the toxin is not expected to be present in the peripheral blood at measurable levels. The recommended quantities of neurotoxin injected at each site should not result in systemic, overt distant adverse effects (i.e., muscle weakness) in patients without neuromuscular disorders. However, sub-clinical systemic effects have been shown by single-fiber



electromyography after IM doses of botulinum toxins appropriate to produce clinically observable local muscle weakness.

#### **BOTOX-Associated Adverse Effects**

##### Treatment of Migraine

When BTX-A is administered as prophylactic therapy for migraine, patients have experienced only minor and transient adverse effects including eyelid and brow ptosis headache, nausea, blepharoptosis, and diplopia. Other BTX-A-associated adverse effects include transient local pain, weakness, and ecchymosis at the injection site.

##### BOTOX-Associated Adverse Effects (in General)

There have been rare, spontaneous reports of death, sometimes associated with dysphasia, pneumonia, and/or other significant disability, after treatment with BTX-A. In addition, there have been rare reports of adverse effects involving the cardiovascular system, including arrhythmia and myocardial infarction, sometimes with fatal outcomes. Some of these patients had risk factors, including cardiovascular disease. The precise relationship of these events to the BTX-A injection has not been established.

The following adverse effects have been reported since the agent has been marketed: skin rash, pruritus, and allergic reaction. These adverse effects have not been definitely attributed to BTX and their causal relationship to the neurotoxin has not been established. The BTX-A preparation contains albumin, a derivative of human blood. Some investigators routinely ask all patients if they are allergic to serum or egg whites, although these investigators acknowledge that they have never seen an allergic reaction to BTX-A. Despite the risks associated with the allergic responses and the potentially life-threatening adverse effects delineated above, there is substantial evidence that BTX-A is a safe therapy when administered in appropriate doses by experienced physicians. BTX-A -associated adverse effects are generally transient, well tolerated by patients, and are amenable to treatment. In general, BTX-A -associated adverse effects occur with the first week following injection of the neurotoxin. These adverse effects are usually transient; however, in some individuals, they may persist for several months. Localized pain, tenderness, and/or bruising may be associated with the injection. Muscular weakness that is localized to the injection site represents the expected pharmacological action of the botulinum toxin. (See PHARMACOKINETICS). Much of this muscular weakness is related to the diffusion of the neurotoxin--or rarely due to inadvertent injection of the toxin--into nearby muscle groups. Generalized muscle weakness, which is characteristic of botulism food poisoning, is rare following BTX-A injections. Systemic complications following BTX-A injection are uncommon. Several studies report that patients treated with BTX-A experience a flu-like syndrome, especially after the initial injection; however, a similar syndrome has been reported in patients who receive placebo injections.

A recently published report describes the occurrence of severe, intractable headache in five individuals who received BTX-A injections (10 U - 120 U) for cosmetic indications. Four of these patients were being treated for glabella, forehead, and/or periorbital creases. The remaining patient was being treated for palmar hyperhidrosis, but had previously received BTX-A injections for glabella and periorbital lines without any evidence of headache. The investigators report that the incidence of severe headache was approximately 1% (5/320). None of the five patients had a history of pre-existing headaches prior to the BTX- injection. The small case series cannot definitely establish a causal relationship between BTX-A injections and severe headache.

In a follow-up study of the BTX-A Glabellar Study Group, 17% and 13 % of patients in the placebo group and BTX-group, respectively, experienced headaches. Thus, BTX-A injection into the glabellar site may increase the risk of subsequent headache, regardless of the solution injected. In addition, the investigators acknowledge that these case reports are from a single dermatologic practice, and that induction of severe headache may therefore be technique-dependent. We are particularly interested in this report that describes the occurrence of severe, intractable headache following BTX-A injection, as our clinical protocol is designed to evaluate BTX-A as prophylactic therapy for migraine headaches.

**Immunogenicity:** Formation of neutralizing antibodies to BTX-A may inactivate the biologic activity of the agent, thereby reducing the effectiveness of BTX-A treatment. Neutralizing antibodies may be one factor associated with therapeutic failure of BTX-A treatments. The rate of formation of these neutralizing antibodies in patients who receive BTX-A has not been well -studied. The critical factors that promote formation of these neutralizing antibodies have

not been well characterized. Results from some studies suggest that injecting BTX-A at frequent intervals and/or at high doses may promote the formation of neutralizing antibodies. Injecting the lowest effective dose of BTX-A at the longest feasible intervals between injections may minimize the potential for antibody formation. The long term (> 5 years) effects of chronic botulinum toxin injections have not been established.

**Warnings:** Individuals with peripheral motor neuropathic diseases or neuromuscular junctional disorders should only receive BTX-A with caution. Patients with neuromuscular disorders may be at increased risk of clinically significant systemic effects including severe dysphagia and respiratory compromise from typical doses of BTX-A. Published medical literature has reported rare cases of BTX-A injection to patients with known or unrecognized neuromuscular disorders where the patients have shown extreme sensitivity to the systemic effects of typical clinical doses. In some of the patients, dysphagia persisted for several months and required placement of a gastric feeding tube.

**Precautions:** Epinephrine should be available or other precautionary methods taken as necessary should a patient have an anaphylactic reaction following BTX-A injection.

**Drug Interactions:** Physicians must exercise caution when BTX-A is being co-administered with aminoglycosides, calcium channel blockers, or other agents that potentiate neuromuscular blockade or interfere with neuromuscular transmission. These other drugs can potentiate the effect of BTX-A.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Subjects are simultaneously screened for the migraine and tension studies. A total of (80) subjects have been screened. Of the (80) subjects screened 75 met criteria for migraine headaches. Thirty two subjects were enrolled and (20) subjects have now completed the study.

The number of subjects enrolled to the study since last APR at WRAMC is 13 and the total enrolled to date at WRAMC is 32.

#### CONCLUSIONS

No conclusion has been established to date. Interim data analysis will be completed once a total of 40 patients have been enrolled.

## DETAIL SUMMARY SHEET

TITLE: "Effectiveness of Botulinum Toxin Type-A in the Treatment of Chronic Tension-type Headache: A Randomized Controlled Trial"

KEYWORDS: Headache, Botox

PRINCIPAL INVESTIGATOR: Labutta, Robert, COL, MC;

ASSOCIATES: Jabbari, Bahman, COL, MC; Murray, Evan, MAJ, MC; Kudelko, Kenneth, CPT, MC; Petit, Cynthia MSN, CRNP

DEPARTMENT: Neurology  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 26 September 2000

### STUDY OBJECTIVE:

It is hypothesized that patients who receive injections of Botulinum toxin A (BTX-A) into selected pericranial muscles can experience a significant reduction in the frequency of headaches and/or the average severity of attacks. We intend to evaluate the efficacy of BTX-A in the treatment of chronic tension-type headache.

### TECHNICAL APPROACH:

This study is a prospective, randomized, double blind, placebo-controlled trial that compares the efficacy of BTX-A injections with placebo in tension type headache prevention. Patients will record the frequency and intensity of headaches in a daily diary for a 1-month baseline period and for 6 months after they receive a single treatment or placebo dose to selected pericranial muscles. The primary outcome measure is the average frequency of headache days measured during 30-day blocks for six months. The secondary outcome measures are the severity of attacks using a visual analog scale (VAS) from 0-10 (0=no headache pain; 10 =most severe headache pain experienced) and the Migraine Specific Quality of Life Questionnaire (MSQ). No modifications were made to the protocol.

### Scientific Rationale:

(BTX-A) is a purified derivative of the exotoxin produced by the bacteria *Clostridium botulinum*. The neurotoxin attaches to, and crosses, the presynaptic plasma membrane and cleaves SNAP-25, a 25kD protein that is critical for the release of acetylcholine from the synaptic vesicles situated within nerve endings. The agent inhibits the release of vesicle-bound acetylcholine, thereby blocking neuromuscular transmission and causing temporary muscle paralysis. BTX is known to have a blocking action on the parasympathetic nervous system that may also inhibit the release of a number of neurotransmitters and neuropeptides other than acetylcholine, including glutamate, norepinephrine, dopamine, substance P, and calcitonin gene-related peptide. The ability of BTX-A to inhibit the release of acetylcholine at the neuromuscular junction and to reduce muscle tone is well established; however, its mechanism of action in the prevention of headache is less clear.

In patients with tension-type headaches, the central modulation of pain perception may be altered and results in a cycle of hypersensitivity that begins at the peripheral muscle. Botulinum toxin affects intrafusal muscle spindles involved in a sensory feedback loop to the spine and central nervous system and may indirectly alter sensory perception and sensitization.

Results of several recent clinical trials demonstrate that BTX-A is an effective prophylactic agent in the management of migraine. In an open label study, 39/77 (51%) of patients treated with BTX-A had a complete response with mean duration of benefit of 4.1 months. Individuals with low baseline headache frequency were more likely to report a complete response than individuals with high baseline frequency; however, the proportion of patients who noted improvement (complete or partial response) did not depend on the baseline severity or frequency of headache. These results were later confirmed in a double blind, placebo-controlled trial. Previous headache studies used doses of BTX-A that ranged from 25 U to 200 U. Schulte-Mattler et al. used a total dose of 200 U of

BTX-A that was divided equally among the frontal, temporal, occipital and sternocleidomastoid muscles for the treatment of tension-type headache. Only one of eight patients had a treatment-related adverse effect, a transient sensation of slight muscle weakness in the posterior neck. Freund, et al. injected a total dose of 100 units of BTX-A into various painful trigger points along the cervical musculature (splenius capitis, rectus capitis, upper trapezius, semispinalis). None of the 14 patients experienced treatment-related adverse effects at four weeks post-injection.

In a recent multicenter, randomized, placebo-controlled trial that assessed the safety and efficacy of BTX-A for the prevention of migraine, patients received either placebo or a total of 25 U or 75 U of BTX-A, which were divided into bilateral injections into frontalis, temporalis, and corrugator muscles. During a one-month baseline period and for three months following injection, patients kept daily diaries in which they recorded migraine frequency, migraine severity, and the occurrence of migraine-associated symptoms. The primary outcome measure in this trial was the frequency of headache as reported by patients in a headache diary. Both doses of BTX-A are significantly superior to placebo in decreasing the number and severity of migraine attacks per month. In addition, patients receiving the BTX-A use less acute migraine medications and experience less migraine-associated vomiting than individuals who received the placebo. The therapeutic index of the 25-unit dose is superior to that of the 75-unit dose. The larger dose is more likely to cause transient paralysis of the levator palpebrae superioris and is associated with a higher incidence of transient ptosis and diplopia. The only BTX-A -associated adverse effects noted in this trial were two cases of transient diplopia and 11 cases of injection site tenderness.

Another double blind, placebo-controlled study demonstrated that BTX-A could reduce the pain intensity of migraine attacks; however, in this trial, BTX-A therapy did not result in a significant reduction in the frequency or duration of migraine attacks. In this trial, patients with IHS-defined migraine were randomized to one of the following injection groups: Group I--BTX-A to the frontal and temporal regions; Group II--BTX-A to the frontal region, placebo to the temporal region; Group III--BTX-A to the temporal region, placebo to the frontal region; and Group 4--Placebo to the frontal and temporal regions. Follow-up data were collected at 2- 4- 8-12-, and 16-week post injection visits from patient diaries that contained the following information: occurrence of migraines, start/stop times of migraines, severity of migraines, migraine associated symptoms, and use of acute migraine medication. Primary outcome measures were frequency, duration, and pain intensity compared with baseline. Group I vs. Group IV at week 12 was defined as the key comparison. Group I maximum pain decrease was significantly greater than for Group IV. Groups I and II experienced greater decreases in migraine duration than Groups III and IV; however, these differences were not significant. There were no discernible differences by treatment group in decrease of migraine frequency, vomiting, or number of migraine day. The investigators concluded that there was a definite trend for BTX-A superiority in reduction of migraine frequency and duration; however, the study lacked adequate power to demonstrate that BTX-A was significantly superior to placebo.

In addition, the results of a recent retrospective study revealed that BTX-A is an effective prophylactic therapy for migraine. The primary outcome measure of this study was relief--defined (by patients) as a reduction in the frequency and our severity of headache attacks. Twenty-three patients had relief that lasted from two to six months. The improvement ranged from a complete elimination of the headaches to a 50% reduction in severity (with unchanged frequency). Four individuals noted no change in the frequency/severity of their attacks. Adverse effects noted in this review included headache immediately after the injection (one patient) and nausea in another individual.

BTX-A has also been effective in the acute treatment for migraine. The agent produced a complete response (i.e., elimination of all headache symptoms) in seven of 10 patients within one to two hours after treatment. In addition, a case of status migraine has responded to BTX treatment. This patients' migraine was refractory to usually effective medications and was treated with 25 U of BOTOX at an acupuncture point for migraine. The patient experienced relief within one hour following injection of the toxin and had no further headaches for two months. (The individual's usual attack frequency ranged from 2-4 attacks per month.)

These numerous trials demonstrate that BTX-A is an effective prophylactic therapy for migraine. Additional studies are required to determine the optimal dosage regimen of the agent and to identify the subpopulation of patients with migraine who are most likely to have an excellent response to BOTOX therapy.

#### BTX-A Pharmacokinetics

When BOTOX is administered as an IM injection at recommended doses, the toxin is not expected to be present in the peripheral blood at measurable levels. The recommended quantities of neurotoxin injected at each site should not result in systemic, overt distant adverse effects (i.e., muscle weakness) in patients without neuromuscular disorders. However, sub-clinical systemic effects have been shown by single-fiber electromyography after IM doses of botulinum toxins appropriate to produce clinically observable local muscle weakness.

#### BOTOX-Associated Adverse Effects

##### Treatment of Migraine

When BTX-A is administered as prophylactic therapy for migraine, patients have experienced only minor and transient adverse effects including eyelid and brow ptosis, headache, nausea, blepharoptosis, and diplopia. Other BTX-A-associated adverse effects include transient local pain, weakness, and ecchymosis at the injection site.

##### BOTOX-associated Adverse Effects (in General)

There have been rare, spontaneous reports of death, sometimes associated with dysphasia, pneumonia, and/or other significant disability, after treatment with BTX-A. In addition, there have been rare reports of adverse effects involving the cardiovascular system, including arrhythmia and myocardial infarction, sometimes with fatal outcomes. Some of these patients had risk factors, including cardiovascular disease. The precise relationship of these events to the BTX-A injection has not been established.

The following adverse effects have been reported since the agent has been marketed: skin rash (including erythematous multiform, urinary and psoriasiform eruption), pruritis, and allergic reaction. These adverse effects have not been definitely attributed to BTX and their causal relationship to the neurotoxin has not been established.

The BTX-A preparation contains albumin, a derivative of human blood. Some investigators routinely ask all patients if they are allergic to serum or egg whites, although these investigators acknowledge that they have never seen an allergic reaction to BTX-A.

Despite the risks associated with the allergic responses and the potentially life-threatening adverse effects delineated above, there is substantial evidence that BTX-A is a safe therapy when administered in appropriate doses by experienced physicians. BTX-A -associated adverse effects are generally transient, well tolerated by patients, and are amenable to treatment.

In general, BTX-A -associated adverse effects occur within the first week following injection of the neurotoxin. These adverse effects are usually transient; however, in some individuals, they may persist for several months. Localized pain, tenderness, and/or bruising may be associated with the injection. Muscular weakness that is localized to the injection site represents the expected pharmacological action of the botulinum toxin. (See PHARMACOKINETICS). Much of this muscular weakness is related to the diffusion of the neurotoxin--or rarely due to inadvertent injection of the toxin-- into nearby muscle groups. Generalized muscle weakness, which is characteristic of botulism food poisoning, is rare following BTX-A injections.

Systemic complications following BTX-A injection are uncommon. Several studies report that patients treated with BTX-A experience a flu-like syndrome, especially after the initial injection; however, a similar syndrome has been reported in patients who receive placebo injections.

A recently published report describes the occurrence of severe, intractable headache in five individuals who received BTX-A injections (10 U - 120 U) for cosmetic indications. Four of these patients were being treated for glabella, forehead, and/or periorbital creases. The remaining patient was being treated for palmar hyperhidrosis, but had previously received BTX-A injections for glabella and periorbital lines without any evidence of headache. The investigators report that the incidence of severe headache was approximately 1% (5/320). None of the five patients had a history of pre-existing headaches prior to the BTX- injection. The small case series cannot definitely establish a causal relationship between BTX-A injections and severe headache.

In a follow-up study of the BTX-A Glabellar Study Group, 17% and 13 % of patients in the placebo group and BTX-group, respectively, experienced headaches. Thus, BTX-A injection into the glabellar site may increase the risk of subsequent headache, regardless of the solution injected. In addition, the investigators acknowledge that these case reports are from a single dermatologic practice, and that induction of severe headache may therefore be technique-dependent.

We are particularly interested in this report that describes the occurrence of severe, intractable headache following BTX-A injection, as our clinical protocol is designed to evaluate BTX-A as prophylactic therapy for migraine headaches.

#### Immunogenicity

Formation of neutralizing antibodies to BTX-A may inactivate the biologic activity of the agent, thereby reducing the effectiveness of BTX-A treatment. Neutralizing antibodies may be one factor associated with therapeutic failure of BTX-A treatments. The rate of formation of these neutralizing antibodies in patients who receive BTX-A has not been well -studied.

The critical factors that promote formation of these neutralizing antibodies have not been well-characterized. Results from some studies suggest that injecting BTX-A at frequent intervals and/or at high doses may promote the formation of neutralizing antibodies. Injecting the lowest effective dose of BTX-A at the longest feasible intervals between injections may minimize the potential for antibody formation. The long term (> 5 years) effects of chronic botulinum toxin injections have not been established.

#### Warnings

Individuals with peripheral motor neuropathic diseases (e.g., amyotrophic lateral sclerosis, or motor neuropathy) or neuromuscular junctional disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome) should only receive BTX-A with caution. Patients with neuromuscular disorders may be at increased risk of clinically significant systemic effects including severe dysphagia and respiratory compromise from typical doses of BTX-A. Published medical literature has reported rare cases of BTX-A injection to patients with known or unrecognized neuromuscular disorders where the patients have shown extreme sensitivity to the systemic effects of typical clinical doses. In some of the patients, dysphagia persisted for several months and required placement of a gastric feeding tube.

#### Precautions

Epinephrine should be available or other precautionary methods taken as necessary should a patient have an anaphylactic reaction following BTX-A injection.

#### Drug Interactions

Physicians must exercise caution when BTX-A is being co-administered with aminoglycosides, calcium channel blockers, or other agents that potentiate neuromuscular blockade or interfere with neuromuscular transmission (i.e., curare-like compounds). These other drugs can potentiate the effect of BTX-A.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Subjects are simultaneously screened for the migraine and tension studies. A total of 80 subjects have been screened. Of the 80 subjects screened 5 met criteria for tension headaches. Three (2) subjects were enrolled and one (1) subject has now completed the study.

The number of subjects enrolled to the study since last APR at WRAMC is 1 and the total enrolled to date at WRAMC is 2.

#### CONCLUSIONS

No conclusion has been established to date. Interim data analysis will be completed once a total of 40 patients have been enrolled.

## DETAIL SUMMARY SHEET

TITLE: A Prospective Study of Stress in Army Reservists

KEYWORDS: Army Reservists Occupational Stress; Longitudinal Study

PRINCIPAL INVESTIGATOR: LTC Elmer W. Combs

ASSOCIATES: Jacqueline Agnew, Ph.D.

DEPARTMENT: Nursing

SERVICE: Nursing Research

STATUS: O

INITIAL APPROVAL DATE: 16 May 2000

### STUDY OBJECTIVE

The overall goal is to apply the newly developed Reserve-Specific Stress Inventory to a cohort of selected reservists in a prospective study design. This will allow the identification of stressors related to reserve, civilian job, and family roles that are associated with adverse health outcomes. The subscales of the Inventory will enable examination of individual and organizational factors that mitigate stress under high stressor conditions.

### TECHNICAL APPROACH

This study will be prospective in design, with each subject followed at six-month intervals for one year following an initial data collection session. Participants will be volunteers who have been randomly selected from unit rosters of Army Reserve units belonging to the 99<sup>th</sup> Regional Support Command in Pittsburgh. After enrolling in the study and providing signed information consent, reservists will be interviewed by telephone using a survey that will address their roles as reservists, civilian workers, students (if applicable), and family members as well as psychological health factors. The newly developed Reserve-Specific Stress Inventory will be used to assess specific stressors as well as personal and organizational resources that can mitigate stress. Outcomes will emphasize injury and stress-related experiences. The data to be collected by interview will measure components of the model that relate to the conceptual framework of the study, i.e. the demand-control model. Because of the geographic dispersion of units and need to distribute initial contact over time, subjects will be enrolled over a period of six months at the rate of approximately 30 participants per month. Total anticipated enrollment: n = 180.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been little activity on this study since the last APR. The post-doctoral student who was working on this study departed in April of 2002. A new student arrived in September of 2002. COL Agnew, an Army Reservist who is primarily responsible for the day-to-day operation of this study, has been called to active duty in Operation Iraqi Freedom (OIF). The TriService Nursing Research Program has granted COL Agnew's request to place this study "on hold" as of 21 March 2003 until further notice. COL Agnew lists difficulty in recruitment due to high levels of mobilization due to the attacks in September of 2001 and OIF, and the lack of an alternate person to assume the role of PI at the institution as reasons for this request.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

Due to deployment of COL Agnew, this study is on hold until further notice.

## DETAIL SUMMARY SHEET

TITLE: Ethical Issues in Department of Army Nursing Practice

KEYWORDS: ethical issues, nursing practice, instrument development

PRINCIPAL INVESTIGATOR: LTC Laura Brosch, AN

ASSOCIATES: COL Janet Harris, AN; LTC (Ret) Janice Agazio, AN

DEPARTMENT: Nursing

STATUS: C

SERVICE: Nursing Research

INITIAL APPROVAL DATE: 11 July 2000

### STUDY OBJECTIVE

The aims of this study are: 1) identify the ethical issues experienced by Army Nurse Corps (ANC) officers and Department of the Army civilian (DAC) registered nurses (RNs) in their practices and the frequency of their occurrence; 2) identify how disturbed ANC and DAC RNs are by these ethical issues; and 3) determine the ethics education needs of ANC and DAC RNs.

### TECHNICAL APPROACH

This study involves two phases. In phase I, focus groups will be used to identify and incorporate Department of the Army and military environment-specific ethical issues into the Ethical Issues Scale. Participants for the focus groups will include ANC officers in TOE units and both ANC and DAC RNs in Medical Treatment Facilities and TOE units. Approximately 30 minutes will be required to complete the survey. Ordinal level data will be analyzed with frequency and contingency tables. Interval level data will be described with means, ranges, and standard deviations, as appropriate. Nonparametric, Chi-Square, will be used to determine if there is a significant difference in the issues experienced by ANC officers and DAC RNs. This study will provide information about the ethical issues experienced in the workplace by ANC and DAC RNs. There were no modifications to the methodology.

### PRIOR AND CURRENT PROGRESS

Three focus groups have been conducted, one at Dewitt Army Community Hospital at Fort Belvoir and two focus groups at Fort Bragg. The 23 participants in the focus groups included ANC officers in TOE units and both ANC and DAC RNs in Medical Treatment Facilities. The tapes of the focus groups have been transcribed and analyzed. Additional items are being added to the Ethical Issues Scale. The revised EIS was distributed to six WRAMC nurses as a pilot test. Phase I is completed. Phase II is underway, including mailing the anonymous EIS questionnaire to all ANCs and DAC RNs in MTFs and TOE units. No adverse events occurred in this study.

The number of subjects enrolled in Phase 1 of the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC (DeWitt) is 14. The total number enrolled study-wide is 29, if multi-site study. In Phase 2, EIS questionnaires were mailed, 564 to WRAMC and 1328 to NARMC. The number of questionnaires mailed since last APR at WRAMC is 243, and 482 to NARMC. The total number of questionnaires mailed study-wide is 5283 if multi-site study. The questionnaire is anonymous, so it is not known how many were returned from WRAMC or NARMC. A total of 1899 questionnaires were returned from all sites.

### CONCLUSIONS

The mean age of respondents was  $41.04 \pm 10.18$  years. 957 respondents indicated they were active duty compared to 824 DAC RNs (1781 out of 1899 participants responded to this question.) Thirty-one percent of respondents reported encountering an ethical issue at least monthly. The two most frequently occurring ethical issues in nursing practice were "protecting patient's rights" and "human dignity" (34.7%) and "staffing patterns that affect quality of patient care" (32.6%). The ethical issue reported as most disturbing were staffing patterns that affect quality of patient care and triaging soldiers to the expectant category.



## DETAIL SUMMARY SHEET

**TITLE:** A Prospective Study to Evaluate the Testing of Individual Donor Units from Voluntary Blood Donation for the Presence of HIV-1/HCV RNA

**PRINCIPAL INVESTIGATOR:** LTC Francisco J Rentas, MS

**ASSOCIATES:** Sherri S. Hall, GS-10, MAJ Michael J. Lopatka, MS

**DEPARTMENT:** Fort Knox, KY

**STATUS:** C

**SERVICE:**

**INITIAL APPROVAL DATE:** 20 June 2000

### STUDY OBJECTIVE

The overall study objective was to collect scientific data from individual donor samples with documented serological assay results for anti-HIV and anti-HCV in support of the intended use of the TMA HIV-1/HCV Assay. TMA results will be compared to results from licensed antibody (HIV-1 and HCV) and p24 Ag (HIV) tests. The primary objective is to determine whether the TMA HIV-1/HCV Assay allows earlier detection of HIV-1/HCV infection than serological screening tests. This clinical study was a collaboration between Camp Memorial Blood Center (CMBC) and Gen-Probe Inc., San Diego, CA.

### TECHNICAL APPROACH

Blood donations from allogeneic volunteers accepted at approved military collection centers were included. Blood was screened for anti-HIV, HIV p24 Ag, and anti-HCV. The TMA HIV-1/HCV Assay was used to test plasma samples and results were compared to the screening results. Donors who tested TMA HIV-1/HCV positive were added to the follow-up study. Follow-up for HCV reactive donors is monthly for one year; for HIV reactive donors it is weekly for three months, or when seroconversion occurs. Follow-up also will take place for any seropositive samples resulting in a non-reactive or equivocal final TMA Assay result. This plasma is shipped frozen to Gen-Probe for an alternate NAT test. All NAT data was released to Gen-Probe Inc. for incorporation into demographic studies. Gen-Probe analyzed the data and forwarded their findings to the FDA to support licensing of this test. There has been one Amendment approved by the WRAMC IRB on 13 November 2001.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 3,045 and the total enrolled to date is 30,780. There were zero adverse reactions. CMBC has not identified any cases where a donor tests TMA positive, EIA negative. These donors would be placed in the follow-up study to determine seroconversion status. The advantage would be in the earlier detection of an HIV/HCV positive donor, thus increasing safety of the military blood supply.

### CONCLUSIONS (this year's)

TMA Reactive Results	Number	TMA Interpretation At Index	Seroconversion Upon Follow-Up		
TMA HIV-1/HCV Reactive Donors	20				
TMA Initial Reactive Only	15	True Neg			
TMA Multiplex (RR) Non-Discriminated	0	Equivocal			
TMA Reactive Discriminated	2				
TMA (Reactive)/Sero Pending	0	Not interpretable			
TMA (R)/Sero (Pos)	2	True Pos			
TMA (R)/Sero (Indeterm)	0	True Pos			
TMA Reactive/Sero Negative	0				
TMA (R)/Alternative NAT (R)	0	True Pos	yes	0	True Pos
			no	0	True Pos
TMA (R)/Alternative NAT (NR)	3	False Pos	yes	0	True Pos
			no	3	False Pos
TMA (R)/No Alternative NAT	0	False Pos	yes	0	True Pos
			no	0	False Pos

Work Unit # 00-8101 [Continued]

Serology Reactive Results with Procleix Nonreactive	Number	TMA Interpretation At Index
EIA Repeat Reactive	8	
Supplemental Pending (or QNS)	0	Not Interpretable
Supplemental Negative	6	True Neg
Supplemental Indeterminate	2	
Alternative NAT (R)	0	False Neg
Alternative NAT (NR)	1	True Neg
Alt NAT Pending (or QNS)	1	Not Interpretable
Supplemental Positive	0	
Alternative NAT (R)	0	False Neg
Alternative NAT (NR)	0	True Neg
Alt NAT Pending	0	Not Interpretable

Of the 20 TMA HIV-1/HCV Reactive donors, 2 were seropositive by Enzyme Immunoassay (EIA) Testing. Both of these donors confirmed positive by supplemental testing.

There were 15 samples that initially tested TMA reactive, but were negative upon repeat TMA testing (false positive). There were 3 samples that initially tested TMA reactive and discriminated positive, but were alternate NAT negative and sero-negative by EIA (false positive). Follow-up testing of 2 of these 3 was negative (false positive). The third donor refused consent for follow-up. There were 8 cases where the EIA test was reactive with a non-reactive TMA result (2 anti-HCV and 6 anti-HIV). Supplemental RIBA 3.0 testing indicated that 0 confirmed positive, 0 were indeterminate, and 2 confirmed negative for HCV. Supplemental Western Blot testing for the 6 HIV cases indicated 2 were indeterminate and 4 confirmed negative. There were 0 HIV confirmed positive cases that were TMA negative. For the HIV indeterminate cases, a frozen sample was sent to a reference lab for alternate NAT testing. All results have returned with 0 positives for HIV. The one tested for alternate NAT was negative, indicating the specimen is a true negative and the EIA reaction was a false positive test. One specimen had insufficient quantity for alternate NAT testing and was not interpretable. There were 0 donors who confirmed positive for HIV or HCV through TMA testing alone.

CONCLUSIONS (overall study)

TMA Reactive Results	Number	TMA Interpretation At Index	Seroconversion Upon Follow-Up		
TMA HIV-1/HCV Reactive Donors	94				
TMA Initial Reactive Only	58	True Neg			
TMA Multiplex (RR) Non-Discriminated	0	Equivocal			
TMA Reactive Discriminated	33				
TMA (Reactive)/Sero Pending	0	Not interpretable			
TMA (R)/Sero (Pos)	32	True Pos			
TMA (R)/Sero (Indeterm)	1	True Pos			
TMA Reactive/Sero Negative	0				
TMA (R)/Alternative NAT (R)	0	True Pos	yes	0	True Pos
			no	0	True Pos
TMA (R)/Alternative NAT (NR)	3	False Pos	yes	0	True Pos
			no	3	False Pos
TMA (R)/No Alternative NAT	0	False Pos	yes	0	True Pos
			no	0	False Pos

Work Unit # 00-8101 [Continued]

Serology Reactive Results with Procleix Nonreactive	Number	TMA Interpretation At Index
EIA Repeat Reactive	119	
Supplemental Pending (or QNS)	2	Not Interpretable
Supplemental Negative	86	True Neg
Supplemental Indeterminate	30	
Alternative NAT (R)	0	False Neg
Alternative NAT (NR)	15	True Neg
Alt NAT Pending (or QNS)	16	Not Interpretable
Supplemental Positive	1	
Alternative NAT (R)	0	False Neg
Alternative NAT (NR)	0	True Neg
Alt NAT Pending	1	Not Interpretable

Of the 94 TMA HIV-1/HCV Reactive Donors, 33 were seropositive by Enzyme Immunoassay (EIA) Testing. Thirty-two of these donors confirmed positive by supplemental testing. One donor was indeterminate. There were 58 samples that initially tested TMA reactive, but were negative upon repeat TMA testing (false positive). There were three samples that initially tested TMA reactive and discriminated positive, but were alternate NAT negative and sero-negative by EIA (false positive). Follow-up testing of two of these three was negative (false positive). The third donor refused consent for follow-up. There were 119 cases where the EIA test was reactive with a non-reactive TMA result (68 anti-HCV, 49 anti-HIV, and 2 HIV p24 Ag). Supplemental RIBA 3.0 testing indicated that one confirmed positive, twelve were indeterminate, and fifty-five confirmed negative for HCV. Supplemental Western Blot testing for the 51 HIV cases indicated 18 were indeterminate and 31 confirmed negative. Two were quantity insufficient for testing and are pending confirmation. There were zero HIV confirmed positive cases that were TMA negative. For all HCV and HIV indeterminate cases, a frozen sample was sent to a reference lab for alternate NAT testing. All results have returned with no positives for HCV or HIV. All those tested for alternate NAT were negative, indicating the specimen is a true negative and the EIA reaction was a false positive test. Five specimens had insufficient quantity for alternate NAT testing and are not interpretable. There were no donors who confirmed positive for HIV or HCV through TMA testing alone.

## DETAIL SUMMARY SHEET

TITLE: Tele-Psychiatry in the Division - A Study of Diagnostic Reliability and Cost Benefits Using Desktop VTC

KEYWORDS: Tele-Psychiatry, Tele-Mental Health, VTC, Diagnostic Reliability  
PRINCIPAL INVESTIGATOR: Johnson, Robert CPT MS

DEPARTMENT: Landstuhl Regional Medical Center  
SERVICE: Division Mental Health

STATUS: O  
INITIAL APPROVAL DATE: 18 July 2000

### STUDY OBJECTIVE

- Determine the diagnostic agreement of clinical psychiatric examinations using in-person, face-to-face evaluations vs. VTC evaluations at a 384kb connection.
- Explore patient satisfaction with examinations using VTC
- Estimate the cost (direct, lost productivity, and lost time) savings of using VTC vs. traditional face-to-face consultations.

### TECHNICAL APPROACH

Each patient enrollment will involve initial brief and consent. The division mental health staff at the Schweinfurt clinic will recruit patients. Only patients that are being evaluated in the clinic will be recruited. Upon completing initial intake evaluation in the Schweinfurt clinic for both command and self referred patients, if, in the view of the provider seeing the patient, a medication evaluation is warranted for the patient, the provider will at that time inform the patient regarding the study being conducted in the clinic. If they say yes, they will be scheduled for an f/u appointment with another provider in the clinic on the same day that they will perform the SCID examination. That provider will perform the informed consent prior to the patient beginning the study.

Patients who have been identified as warranting a medication evaluation will have an appointment set up for them with one of the mental health technicians at the Schweinfurt clinic who has not been involved with their treatment to date. This appointment will occur on the same day that the provider who is performing the SCIDs is available. Because there are only 4 providers in the clinic and the recruitment of patients will be coming from each of the provider's patient load, we will be unable to have only one person perform all informed consent, as it would disqualify all of his or her patients from the opportunity to enroll in the study. The NCOIC of the clinic will be responsible for scheduling all of the patients identified as potential candidates for the study for both the informed consent meeting and the subsequent SCID evaluation. The patient will then be administered the SCID. The patient will also be asked to fill out an O-Q (outcome questionnaire) at the time of SCID. Neither psychiatrist will know the results of the SCID until after the patients participation in the study has ended. After the initial evaluation, one of the two psychiatrists will be assigned as the primary provider for the patients requiring follow up. The results of the SCID and the O-Q can be made known to them. Patients will then be assessed by Psychiatrist #1 using either face-to-face or VTC as outlined above. Psychiatrist #2, who will be blinded to the results of the previous exams, will then see the patients. Psychiatrist #2 will use the opposite interviewing technique of psychiatrist #1 (VTC or face-to-face). After each assessment, the clinician will document a maximum of two diagnoses and a GAF (global assessment of function) score. The psychiatrist seeing the patient in person will be responsible for the clinical note and chart maintenance and will render the actual clinical diagnosis for the patient's active chart. The GAF is part of the routine psychiatric Axis I-V diagnostic framework. At the end of the interviews, the patient will be given an evaluation sheet to collect demographic information to help evaluate costs and to document patient satisfaction with the VTC experience. The patients will be asked to complete a satisfaction survey using a 10cm visual analog scale following each interview.

Patients will then be released from the clinic unless clinical intervention is warranted. The psychiatrist who saw them in person will follow patients evaluated for medications who actually need medication treatment. The results of the SCID and tele-psychiatry evaluation will be made known to the provider prior to the first follow up appointment in order to help the provider confirm his diagnosis, which could be beneficial to the patient.

The SCID has been shown to have excellent interater agreement for broad diagnostic categories such as Psychotic disorders (kappa, 1.00), mood disorders (kappa, .93), anxiety disorders (kappa, .82) and substance use disorders (kappa, .93). Reliability was as follows for specific diagnoses; schizophrenia (kappa, .94), major depression (kappa, .93), dysthymia (kappa, .88), generalized anxiety disorder (kappa, .95), panic disorder (kappa, .88), alcohol use disorder (kappa, .96), cyclothymia (kappa, .80), PTSD (kappa, .77), bipolar disorder (kappa, .79), adjustment disorder (kappa, .74), and obsessive-compulsive disorder (kappa, .40). 10 Few studies exist comparing diagnostic reliability between the SCID and a routine psychiatric evaluation. One study by Fennig et al (1994) showed agreement as follows for an initial evaluation; major depression (kappa .75), schizophrenia (kappa .86), and bipolar disorder (kappa .89).

The OQtm-45.2 has been shown to have a test-retest reliability correlation coefficient of 0.84. In an outpatient psychiatric clinic population it was found to have validity ranging from 0.71 to 0.84.12.

The GAF scale has been shown to have a validity of -0.73 when compared to other Zung Depression Scale. The original GAF has an interater reliability of .62. A modified version of the GAF has a higher interater reliability of 0.81. The authors of this scale and the study comparing the original GAF to the modified GAF suggested that the modified GAF might be a better scale to use in research protocols. The correlation between the original GAF and the modified GAF was shown to be high (0.80).

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR is 0 and the total enrolled to date at WRAMC is 3.

#### CONCLUSIONS

Conducting this study in a Division setting has been extremely challenging, given the requirements of three doctoral level mental health providers. Over the past 24 months, due to deployments, PCS moves, etc., this requirement has not been fulfilled, so research has yet to begin. With the return of the Division Psychiatrist from Kosovo in May of 2003, it is likely that the research protocol will be underway within the next sixty to ninety days.

## DETAIL SUMMARY SHEET

TITLE: Genetic Investigations of Pseudofolliculitis Barbae, (PFB), in United States Armed Forces

PRINCIPAL INVESTIGATOR: MAJ Daniel J. Schissel, MC

DEPARTMENT: Landstuhl Regional Medical Center  
SERVICE:

STATUS: C  
INITIAL APPROVAL DATE: 15 August 2000

STUDY OBJECTIVE:

This study will investigate the association of PFB with the cytokeratin K6hf mutation found in the hair follicle.

TECHNICAL APPROACH:

The protocol is designed as a stratified case-control study with the aim of determining the relative risk of the mutation for the occurrence of cutaneous problems among shaving persons. Within each stratum, one investigates a group of PFB cases and a control group who do not exhibit the skin condition when shaving. The prevalence of the mutation is estimated to be greater than 80% among PFB cases, and to be less than 10% among controls.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

An unusual Ala12Thr polymorphism in the 1A  $\alpha$ -helical segment of the companion layer-specific keratin K6hf is a significant risk factor for the common hair disorder Pseudofolliculitis barbae.

Running title: Pseudofolliculitis and keratin mutations

(The opinions expressed in this paper are those of the authors and should not be construed as official or as representing those of the United States Air Force, United States Army Medical Department or the United States Department of Defence).

**Abstract.** Pseudofolliculitis barbae, PFB, is a common hair disorder characterized by a pustular foreign body inflammatory reaction that is induced by ingrown hairs of the facial and submental (barbae) regions after regular shaving. PFB occurs predominantly in black males while it is rather rare and usually far less severe in caucasian males. Black individuals have a higher propensity of developing PFB due to their genetic predisposition for curly hair that inherently possesses a much higher risk of growing back into the skin than does straight or wavy hairs. The PFB process is, however, not gender dependent or restricted to the face, but can occur in any skin region once regular shaving, plucking, or other traumatic means of hair removal are instituted. Through a family study and a large scale investigation of randomly sampled PFB-affected and -unaffected individuals this study demonstrates that unlike all other skin keratinopathies, an unusual single nucleotide polymorphism, which gives rise to a disruptive Ala12Thr substitution in the 1A  $\alpha$ -helical segment of the companion layer-specific keratin K6hf of the hair follicle, is partially responsible for the phenotypic expression and represents an additional genetic risk factor for PFB.

**Introduction.** Pseudofolliculitis barbae (PFB), also termed *pili incarnati* or "ingrown hairs", is a common human hair disorder that occurs on the neck and the submental region of the face. Regular shaving, in particular "against the grain", represents the precipitating factor in this disease. The razor produces short, sharp, and pointed hairs that penetrate the skin either in an extra- or transfollicular manner. These ingrown hairs initiate a foreign body reaction producing erythematous papules and pustules that may heal with or without scarring and may even produce keloid formation. The primary lesions normally subside upon discontinuance of shaving or employing alternative grooming measures (Dubreuilh, 1922; Strauss and Kligman, 1956). Compared to caucasian males, black males are distinctly more susceptible to developing PFB due to their genetic predisposition for strongly curved hairs. These hairs show a concavity towards the epidermis and therefore have a much higher tendency to reenter the skin than straight or wavy hairs (Strauss and Kligman, 1956; Rook and Dawber, 1982; Kauvar, 2000). Furthermore, facial hair patterns have

recently been identified as an additional genetic factor involved in the PFB process. Normally, the direction of beard hair growth is caudal. Cephalic directed hair patterns or those in whorls or small eddies have been found to initiate localized PFB after shaving (Pinkus, 1927; Ross *et al.*, 1993). PFB reactions after regular shaving have, however, also been noted in the scalp of black males, the axillary and pubic skin region and on the legs of black and Asian women as well as on the face of women suffering from hirsutism (Crutchfield, 1998; Smith and Odom, 1977; Alexander, 1974; Dilaimy 1974; Garcia and White, 1978; Hage and Bourman, 1991). The present investigation demonstrates a disruptive Ala12Thr substitution, which occurs as a single nucleotide polymorphism in the 1A  $\alpha$ -helical subdomain of the hair follicle companion layer-specific keratin K6hf (Winter *et al.* 1998) and its role as an additional genetic risk factor for the development of PFB.

**Methods. Patients.** One pedigree indicates a three-generation caucasian family whose male members I-2 (deceased), II-2 and III-2 suffered from relatively severe PFB symptoms, while female individuals I-1, II-1 and III-1 denied hair problems of any kind (for details, see Results). The majority of male and female PFB patients and unaffected individuals used in a large-scale study were recruited from the United States Army Hospitals in Heidelberg and Landstuhl, Germany. Additional test persons were recruited from the German Cancer Research Center as well as a local general medicine clinic. All individuals were initially educated on the clinical aspects of PFB. After a historical review for PFB symptoms associated with regular shaving practices (at least once per week) of the beard, axilla, groin or leg region, individuals were assigned either to an unaffected or an affected group. PCR and automated DNA sequencing. After Ethics Committee approval, samples of approximately 20 plucked scalp hairs, each obtained from individuals II-2, II-3, III-1 and III-2 of the PFB study family, as well as consecutively coded peripheral blood probes, drawn from the members of the affected and unaffected test groups, were used to extract genomic DNA for analysis by means of the QiAamp blood kit (Qiagen, Hilden, Germany). Mutation analysis for the 1A  $\alpha$ -helical segment of keratin K6hf was performed as described by Winter *et al.*, 1997. Briefly, genomic DNA was PCR amplified using forward primer (exon 1) 5'-TCAGTGGCCCCAGCTTCCCCGTGTGTC-3' and reverse primer (exon 2) 5'-TGTTCCCTCAGTTCAGCTTCAAGCCTG-3'. Direct, automated sequencing of the PCR products was performed according to the Thermo Sequenase radiolabelled chain terminator cycle sequencing protocol (Amersham) using the forward primer. Computer generated models of the K6hf/K17 and hHb6/hHa1 1A segments. The K5/K14 model of Liovic *et al.* 2001, was used as a template for the keratin since it had a very high degree of sequence identity with the structures studied here (approx 93%). Appropriate residue replacements were made in the heterodimer using Turbo-Frodo (Roussel *et al.*, 1998), and minimization and molecular dynamics were then performed using AMBER 7 (Case *et al.*, 2002). Initial minimization was carried out as part of a multi-step process using the method of steepest descents. Heavy atoms, followed by backbone atoms and N- and C-terminal main-chain atoms, were constrained and energy minimized over 100 cycles of steepest descent. The resulting structure was checked with (Hooft *et al.*, 1996) in WHATIF (Vriend, 1990), and gave a similar score to that of the template model. A box of 4862 water molecules was then added to the structure and equilibrated with constrained protein. Particle mesh ewald dynamics calculations were then performed for 400ps at 300K with constraints placed on the main-chain atoms at the N- and C-terminus. Again, scores remained closely similar to those of the starting model. At this point the residue replacement Ala12Thr was made in K6hf and the molecular dynamics calculations repeated.

**Cell culture and transfections.** K6hf and K17 cDNAs were obtained by BamI/HindIII digestion of the previously described bacterial expression vector constructs K6hfpDS5 and K17pDS5, respectively (Hofmann *et al.*, 2002). The K6hf Ala12Thr cDNA was generated by RT-PCR using cDNAs from plucked hair follicles of individual II-2 of the PFB family as a template. After cloning of the various cDNAs into the PCR cloning vector pCR-XL-Topo (Invitrogen) and verification of the correct ORF by sequencing, the cDNAs were cloned into the eukaryotic expression vector pcDNA3.1 (Invitrogen). PtK2 cells (potoroo kidney simple epithelial cells) were cultured in plastic tissue culture grade dishes without feeder cells in a 1:1 mixture of DMEM and Ham's F12 growth medium supplemented with 10% FCS and 1% L-glutamine at 37°C and 5% CO<sub>2</sub>. For transfections, cells were cultured on 13 mm diameter cover slips (BDH) to 50% confluence. Transient transfections were carried out using the FuGene 6 transfections reagent (Boehringer Mannheim) according to the manufacturer's instructions plus 1  $\mu$ g of plasmid DNA per 2 ml of serum free medium. K6hfWT and K6hfAla12Thr plasmid DNAs were mixed at a 1:1 ratio with K17 (K6hfWT/K17 or K6hfAla12Thr/K17) and incubated with the FuGene 6 reagent for 24 hr at 37°C, after which the culture medium was replaced with fresh medium.

**Immunofluorescence and imaging.** Keratin IF formation in PtK2 cells was detected by indirect immunofluorescence, using the previously described K6hf specific guinea pig polyclonal antibody (Winter et al, 1998) and Alexa Fluor 488 goat anti-guinea pig IgG (H+L) (Molecular Probes) as secondary antibody. Cells were fixed and stained for K6hf at fixed time points 24h and 48h after transfections. Images (512x512 dpi, 2x2 binning) were collected using a 100x 1.4 NA oil immersion objective on a Nikon inverted TE200 Eclipse epifluorescence microscope equipped with a fully motorized Z stage (Applied Precision) and linked to a Micromax CCD camera (Roper Scientific), part of the Delta Vision imaging system (Applied Precision).

**Statistical analysis.** Statistical significance was determined by means of Fischer's Exact Test for the comparison of two proportions using the statistical package ADAM of the Biostatistics Unit of the German Cancer Research Center. Results were considered significant if the two-sided p-value was less than 0.05. Conditional logistic regression, odds ratios and their 95% confidence intervals were calculated using the SAS software package. Exact 95% confidence intervals were taken from Geigy tables.

**Results. Patients and mutation analysis.** Initially, we had access to a three-generation caucasian family whose male members, including the deceased individual I-2, possessed distinctly wavy scalp hairs and suffered from relatively severe PFB. The typical primary lesions of papules and pustules were not limited to the neck and submental region, but were also found on the cheek. Moreover, individual II-2 complained of hairs principally on the undersurface of the chin and the neck, that frequently were completely buried in a spiral-like manner within the pustules and occasionally reached a length of about 1 cm when removed. To investigate the potential of mutated keratins that are expressed in compartments of the hair follicle thought to be involved in the correct guidance of the growing hair, we analyzed the critical helix initiation and termination regions of the recently described inner root sheath-specific type II keratin gene K6irs1 (Langbein et al. 2002), as well as the companion layer-specific keratin gene K6hf (Winter et al, 1998) for mutations. While no alterations were found in the K6irs1 gene (results not shown), we identified a heterozygous G→A substitution in a GCC codon of the K6hf gene. This G→A change led to a conservative Ala12Thr substitution in the 1A  $\alpha$ -helical segment of the keratin (Ala161Thr in the total keratin) in affected individuals II-2 and III-2. The K6hf Ala12Thr substitution was not found in the female individual II-3, but was present in female individual III-1. However, both exhibited rather straight hair and neither shaved regularly, nor removed hair by other traumatic means. Indeed, they denied hair problems of any kind. The K6hf Ala12Thr substitution does not interfere with the formation of coiled-coils. Ala12 represents one of the strictly conserved amino acid residues in the 1A helix segments of all type II keratins, suggesting that its substitution potentially compromises the formation of stable intermediate filaments (IFs). This assumption is supported by our recent finding that a non-conservative Ala12Glu mutation in the type II hair cortex keratin hHb6 was causative for monilethrix (Winter et al, 2000). In order to evaluate the effect of both the K6hf Ala12Thr and hHb6 Ala12Glu substitutions, we generated three-dimensional computer models of the normal and mutated 1A coiled-coil domains of the two keratins, using as type I partners the 1A segments of K17 (Trojanowsky et al, 1992), which is co-expressed over a wide range with K6hf in the companion layer (Winter et al, 1998), and hair keratin hHa1 (Rogers et al, 1998), co-expressed with hHb6 in the hair cortex (Langbein et al, 2001). The potential changes induced by the Ala12Thr substitution on the structure of the K6hf 1A coiled-coil were minor and largely confined to a turn of  $\alpha$ -helix either side of residue 12. The axis of the coiled-coil remained straight and the root mean square deviation between the C $\alpha$  positions of the starting and mutated refined structures was small (0.054 nm). In addition, only minor perturbations close to the site of the mutation were also observed upon modeling of the normal and Ala12Glu mutated hHb6 1A segments (results not shown). The K6hf Ala12Thr substitution is disruptive at later stages of filament assembly. The results of our modeling study contrast with pronounced coiled-coil disturbances recently observed upon modeling the sterical effects of a conservative Val18Leu mutation in the 1A segments of both K5 and K14, causing epidermolytic bullosa simplex (Liovic et al, 2001). The reason for this discrepancy probably lies in the position of the critical substitutions within the heptads of the respective 1A segments. While Val18 occupies an internal a position, Ala12 lies in an external b position on the surface of the coiled-coil and is thus well displaced from the area of contact between the two chains that specify molecular assembly. It is therefore conceivable that its substitution does not seriously modify either the  $\alpha$ -helical structure of the 1A segments or their ability to assemble in register in a parallel mode. Knowing of the demonstrated pathogenicity of the hHb6 Ala12Glu monilethrix mutation (Winter et al, 2000), it is evident that the Thr and Glu substitutions of Ala12 in the outer b position of the



1A segments lead to significant localized changes in the surface appearance of the coiled-coil molecules and that this must compromise the aggregation of the keratin molecules in the IF. In order to demonstrate this for the K6hf Ala12Thr substitution, we investigated whether these postulated disturbances of IF formation could be seen in a cell culture system. To this purpose, three expression constructs, containing either K17 or the wild type (WT) and Ala12Thr forms of K6hf were transfected in different combinations into PtK2 cells which express an endogenous K8/K18 IF network (Lane and Klymkowsky, 1982). The combination K6hfWT/K17 forms a fully extended IF system while the combination K6hfAla12Thr/K17 leads to a tight and fragmented network around the nucleus as well as a multitude of cytoplasmic aggregates. Collectively, these data demonstrate that the disruptive K6hf Ala12Thr substitution is autosomal dominantly transmitted in the described PFB family. Nonetheless, no clear and concise answer can be given regarding the segregation of the Ala12Thr substitution in association with the PFB phenotype, as the female members of this family lack any history of traumatically induced hair removal difficulties. Focusing on the male members alone, there is, however, strong evidence that the K6hf Ala12Thr substitution is associated with the PFB disease process.

**Large scale investigations.** Based on these observations, we investigated the frequency of the Ala12Thr substitution in representative groups of phenotypically PFB-affected and -unaffected individuals from individuals in the U.S. Army in Germany. There were two distinct reasons the majority of the sampling (156/200 individuals) took place at two U.S. Army hospitals in Germany. First, the grooming code of U.S. Army guaranteed the access to a sufficiently large population of individuals that must shave regularly to a set standard. Second, considering the low PFB frequency in caucasians, we wanted to increase the number of potentially susceptible individuals through the inclusion of Afro-Americans. Indeed, our randomly sampled test population confirmed a much higher PFB incidence in the black population (82% in black individuals versus 18% in caucasian individuals), which fell within the previously reported variation range of 50% to 83% (Kauvar, 2000). A minority of PFB-affected individuals were black (7%) and caucasian women (3%), who noted PFB symptoms after shaving in the groin and/or the axilla. After informed consent and the isolation of blood DNA, followed by PCR amplification and sequencing of the 1A coding region of the K6hf gene, the frequency of the G→A transition in the Ala12 codon was found to be 9% in group A and 36% in group B. The affected group B demonstrated a statistically significant higher G→A transition rate than that of the unaffected group A ( $p < 0.000006$ ). This statistical significance held true, when the incidence of the resulting Ala12Thr substitution in the two groups was determined separately for males ( $p < 0.0008$ ) and females ( $p < 0.0001$ ). In addition, the relative risk of developing PFB was significantly increased in the presence of the Ala12Thr substitution by a factor of 6.12. Remarkably, our data indicated that the incidence of the Ala12Thr substitution in the investigated population was approximately 3 times higher in the black population than in caucasians (36.7% versus 10.9%). Moreover, in accordance with a previous study (Alexander, 1974), more than 50% of affected black individuals, including women, affirmed that they had fathers or brothers, or both, afflicted with PFB. Subsequent evaluation of the risk factor “curved hair follicle” in the logistic regression of the incidence of PFB in the presence of the K6hf Ala12Thr substitution, not only showed that both represent independent risk factors for the condition, but also revealed a more than 50 times higher risk to develop PFB difficulties in the presence of curly hair.

**Discussion** Based on the segregation of a G→A transition in the Ala12 codon of the K6hf gene which entailed a conservative Ala12Thr replacement at the protein level with the PFB phenotype in male members of a Caucasian three generation family, we investigated the occurrence of the K6hf gene defect in representative, groups of randomly sampled unaffected and affected individuals. In view of the observed frequencies of the G→A transition in the two groups, it is clear that the base substitution must be considered a single nucleotide polymorphism (SNP). To our knowledge, this is the first example of a potentially deleterious keratin gene mutation that has passed beyond the 1% margin through which mutations are per definition, distinguished from SNPs (Brooks, 1999, Kirk et al, 2002). There are multiple reasons that may account for this unusual spread of the K6hf gene defect. First, it is evident that compared to the known plethora of disfiguring and disabling keratinopathies, PFB represents a distinctly minor health problem. Based solely on its symptoms, there is certainly only a negligible social pressure against its spread. Only few examples are known for distressing and discriminating situations related to PFB, i.e. for black men enrolled in the US Army, where a rigid grooming code requires clean-shaven faces and the resulting “razor bumps” are a source of much misunderstanding and social unrest (Conte and Lawrence, 1979; Alexander and Alexander, 1974; Coquilla and Lewis, 1995). Otherwise, affected men have the possibility of either growing a beard

which completely circumvents the outbreak of the disorder, or substantially minimizing PFB symptoms by improvising less traumatic shaving “with the grain”, using razors which avoid both the formation of sharp hair tips or retraction of the cut hair underneath the skin (Crutchfield, 1998). More importantly, however, it has to be taken into consideration that in the female population with a generally low shaving rate, the Ala12Thr polymorphism remains essentially dormant and is thus propagated without knowledge. Collectively, all of these factors contribute to the relatively high incidence of the deleterious K6hf gene defect and its maintenance in the human population. Intuitively then, one questions how the K6hf Ala12Thr polymorphism promotes PFB. The basic follicular anatomy helps us understand the process. The hair shaft is surrounded by the outer root sheath (ORS), the companion layer, and the inner root sheath (IRS). Cells of the companion layer display a particularly striking concentration of prominent intermediate filament (IF) bundles on the side facing the outer Henle cells of the IRS, to which they are tightly connected by numerous desmosomes. This suggests that the companion layer/IRS complex constitutes a functional tissue unit that tightly surrounds the hair shaft and serves to guide and stabilize the ascending hair (Langbein et al, 2002; Niemann and Watt, 2002). It is conceivable that IF-destabilizing mutations in the K6hf keratin may disturb both the mechanical integrity of companion layer cells and their firm attachment to the IRS and thus lead to a functionally compromised companion layer/IRS unit. This compromised unit may no longer be able to tightly guide and protect the hair on its movement to the skin surface. Importantly, most disruptive keratin mutations remain essentially unremarkable as long as the corresponding tissue is not mechanically traumatized (Irvin and McLean, 1999). In the case of the PFB-associated hair follicle, both pressure and traction exerted on the skin by regular and close shaving may represent the mechanical stress that activates the deleterious nature of the K6hf Ala12Thr polymorphism and results in destabilized pointed hairs in the hair channel. These hairs subsequently run a high risk of either getting trapped while still in the hair channel or leaving the follicular orifice in a less than optimal manner and consequently growing back into concave skin areas of the submental or submandibular region. It is evident that the hair-destabilizing effect of the K6hf Ala12Thr polymorphism should generally be more efficient in promoting PFB in the presence of curled rather than straight hair. It is therefore possible that the combination K6hf Ala12Thr/straight hair may remain phenotypically unremarkable in particular if the submental and submandibular skin regions exhibit horizontally oriented hairs that are less able to grow back than caudally oriented hairs. Those apparently not unusual hair patterns (Pinkus, 1927; Ross et al, 1993) may partially account for the relative high number of Caucasian individuals exhibiting the K6hf Ala12Thr substitution in the absence of PFB symptoms. Taken together, our data demonstrate that PFB is an unusually complex disease process whose etiology besides shaving as the mechanical condition *sine qua non*, involves several genetic risk factors. Similar to liver diseases of multiple etiologies ( Ku et al, 2003), one of these risk factors seems to be a defect in a keratin gene. The potentially hair-destabilizing polymorphism observed in the K6hf gene, also requires a mechanical stress like shaving to become activated. Apparently, the effects of both risk factors are then modulated by likewise genetically determined traits such as hair type and patterns, which may either lead to an aggravation or an attenuation of the PFB phenotype.

**Acknowledgements.** We thank Silke Prätzel and Anke Wollschläger, German Cancer Research Center, for excellent technical assistance and Dr: Klaus Kaminski, 69256 Mauer, for sampling blood probes.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 200, if multi-site study.

#### CONCLUSIONS

See above.

## DETAIL SUMMARY SHEET

TITLE: Racial Differences in Central Corneal Thickness Between Caucasian and African-American Subjects

KEYWORDS:

PRINCIPAL INVESTIGATOR: Hess, Todd LTC MC

ASSOCIATES:

DEPARTMENT: Landstuhl Regional Medical Center

STATUS: O

SERVICE: Ophthalmology

INITIAL APPROVAL DATE: 19 September 2000

### STUDY OBJECTIVE

To determine whether there is a clinically significant difference in central corneal thickness as measured by ultrasound between a group of African-American and a group of Caucasian subjects.

### TECHNICAL APPROACH

Corneal applanative pachymetry is performed on subjects after consent and with topical corneal anesthesia. Three measurements are taken per eye and the lowest is recorded. No changes in methodology have occurred since the last APR.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The data has been analyzed and shows that there are race-related differences in central corneal thickness. We are awaiting publication approval before submitting for publication.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 253.

### CONCLUSIONS

See above.

## DETAIL SUMMARY SHEET

TITLE: Skin-Contact Monochromatic Infrared Irradiation on Lateral Epicondylitis

KEYWORDS:

PRINCIPAL INVESTIGATOR: Paul F. Pasquina, MAJ, MC  
ASSOCIATES:

DEPARTMENT: Orthopedics and Rehabilitation  
SERVICE: Physical Medicine & Rehabilitation

STATUS: O  
INITIAL APPROVAL DATE: 22 February 2000

### STUDY OBJECTIVE

Determine whether the pain response after application of Skin-Contact Monochromatic Infrared Irradiation differs from that of placebo in the treatment of lateral epicondylitis.

### TECHNICAL APPROACH

Randomized, double blind, placebo controlled prospective study of active vs. placebo unit. There have been no changes in the technical approach since the last review.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since the last review, there has been only one new recruited subject. The study subject did not have any adverse effect from the treatment. There is no new medical evidence of changes in care based on the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 1 and the total enrolled to date at WRAMC is 6.

### CONCLUSIONS

I would still like to continue with the study, although we continue to have a problem recruiting subjects.

## DETAIL SUMMARY SHEET

TITLE: Comprehensive Prospective Gait Evaluation of Patients with Spinal Cord Pathology

KEYWORDS: Gait Analysis, Spinal Cord Injury, Spinal Cord Pathology

PRINCIPAL INVESTIGATOR: COL Steven Shannon, MC

ASSOCIATES: LCDR Sean Kelly, MC; COL Bahman Jabbari, MC

DEPARTMENT: Orthopedics and Rehabilitation

STATUS: C

SERVICE: Physical Medicine and Rehabilitation

INITIAL APPROVAL DATE: 18 April 2000

### STUDY OBJECTIVE

To describe the gait characteristics of subjects with spinal cord pathology (SCP) during the first year after diagnosis.

### TECHNICAL APPROACH

SCP subjects and controls will be tested with a computerized 3-D gait laboratory including a dynamic EMG machine, and descriptive statistics will be presented and analyzed.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

None.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

### CONCLUSIONS

This study is being closed due to loss of Principle Investigator and because another DSCCIC protocol has taken its place.

## DETAIL SUMMARY SHEET

TITLE: Determination of Low Back Muscle Usage by MRI Before and After Stepper Machine Exercise

KEYWORDS: MRI, exercise, back musculature

PRINCIPAL INVESTIGATOR: LTC Raul Marin MC

ASSOCIATES: MAJ Phil Dinauer MC; MAJ Roberto Perez-Millan MC; LTC Jeffrey Gambel MC; Tamara Cyhan, RN

DEPARTMENT: Orthopedics and Rehabilitation

STATUS: O

SERVICE: Physical Medicine and Rehabilitation

INITIAL APPROVAL DATE: 19 September 2000

### STUDY OBJECTIVE

Compare the effect of two methods of using the stepper machine on the recruitment ("usage") of back muscles in normal subjects using MRI.

### TECHNICAL APPROACH

Male and female subjects between the ages of 18 and 39 years were enrolled. Volunteers were recruited by word of mouth. This was intended to be a prospective, randomized complete block, crossover single blinded trial. Because of our inability to recruit equal numbers of males and females, we were unable to stratify the subjects into gender specific blocks. The order of the stepping method was randomized via a computer generated randomization table.

A baseline MRI (baseline scan # 1) of the gluteal muscles with the subject at rest was performed initially. The radiologist performing the MRI readings was blinded as to the condition (rest, regimen 1, or regimen 2) associated with the films being read. Each subject began exercising in the stepper machine doing either six inch short stepping technique with subject's hands free from the bars so to maintain the upper body weight supported exclusively by the back extensor musculature, or full length stepping technique with subject's hands holding the support bars. A five-minute warm-up preceded the exercise session. Intensity of exercise was determined by the rate of perceived exertion. MRI scanning occurred immediately after this first exercise session (post-exercise scan # 1), followed by a ten-minute rest period. The rest period was followed by a baseline re-test in the MRI scanner (baseline scan # 2). Then the subject began second exercise regimen. Re-scanning followed immediately after this second exercise regimen (post-exercise scan # 2). Thus, each subject was scanned four times (baseline # 1, post-exercise # 1, baseline # 2, post-exercise # 2). The placement of each subject in the MRI table was clearly marked, utilizing bony landmarks to ensure that the subsequent scanning sequences occurred with the subject lying in the exact position as he/she was during the first scanning.

\*Approval of the 29 January 2003 addendum modified the protocol such that the baseline scan #2 was removed from the methodology since there was no difference in gluteal or paraspinal intensity between the first and second baseline MRIs, so a cross-over effect was ruled out and the second baseline MRI was not necessary. The subjects still receive a ten-minute rest to ensure no crossover effect. The consent form was modified to reflect this change. There was also an addition of specific data points at this time: subject handedness, stepper machine intensity level, and subjective statement regarding which technique was more difficult.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 11 and the total enrolled to date at WRAMC is 28. No adverse events occurred. It is not a multi-site study.

Of the patients currently enrolled, six have had MRIs of the paraspinal muscles and 22 have had MRIs of the gluteal muscles. The plan is to perform another statistical analysis when total enrollment reaches 30 subjects to see if the MRI T2 signal intensity of the gluteals shows a significant difference between the two exercise techniques.

A protocol deviation inadvertently occurred when a non-DEERS eligible healthy volunteer participated in the study. The deviation was reported on 23 January 2003 in hopes that the subject's data could be included in the study analysis. The HUC discussed the deviation, and decided that the data from the non-DEERS eligible participant could not be used based on Army regulations that the HUC does not have the authority to grant exceptions. The subject's data was disregarded.

#### CONCLUSIONS

The information we have collected over the past year will be analyzed after we reach our current target goal of 30 subjects. The 22 subjects who obtained MRIs of gluteals will provide for their own control (baseline MRI) as well as determination of the variation of gluteal muscle usage during two distinct stepper techniques.

## DETAIL SUMMARY SHEET

TITLE: Epidemiology of Military Beneficiaries Receiving End-Stage Renal Disease (ESRD) Therapy

PRINCIPAL INVESTIGATOR: Welch, Paul COL MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Nephrology

APPROVAL DATE: 7 November 2000

### STUDY OBJECTIVE:

We sought to characterize the military beneficiary population receiving ESRD therapy. Goals included identifying and describing all prevalent military ESRD patients for 1998, and comparing the military ESRD population with the entire U.S. ESRD population.

### TECHNICAL APPROACH

The 1998 Defense Manpower Data Center (DMDC) database was compared with the United States Renal Data System (USRDS) database to identify military ESRD patients contained within the USRDS cohort registry. Analysis of all military beneficiaries and the military ESRD population was done using SPSS 9.0. Racial distribution for the entire military population was estimated from the 27% of military beneficiaries whose race was known.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This is the second APR since the study was approved. The following are preliminary results of our analysis. 8,177,611 military beneficiaries are listed in the DMDC database for 1998. Compared with the U.S. population, the military beneficiary population is older (mean 38.4 + 23.2 years vs. mean 36.2 for U.S.), predominantly male (53.4% vs. 48.9% for U.S.), has lower proportion whites (77.3% vs. 82.5% for U.S.), and higher proportion blacks (18.2% vs. 12.7% for U.S.). 17,470 military beneficiaries receiving treatment for ESRD were identified in the USRDS. 1,687 (9.7%) died prior to 1998, 1,090 died during 1998, 2,546 started ESRD therapy during 1998, and 4,812 began ESRD therapy after 1998. Point prevalent count (on 12/31/98) was 9,881 and period prevalence count was 10,971. Unadjusted military ESRD incidence (311 per million vs. 320 per million for U.S.) and prevalence (1,208 per million vs. 1,177 per million for U.S.) were similar to the U.S. population. Unadjusted incidence and prevalence by ESRD etiology were also similar. ESRD incidence ratios (black vs. white) were 1.58 in military vs. 3.10 for U.S., and prevalence ratios were 2.16 in military vs. 3.58 for U.S.. Reduced racial disparity appeared to be due to lower incidence and prevalence of ESRD in black military beneficiaries. Based on period prevalence and average U.S. costs for ESRD care, \$476,657,030 was spent caring for military ESRD patients in 1998. Since the last APR, we have been attempting to find ways to better estimate the racial mix of the military population in the USRDS in order to calculate adjusted incidence and prevalence. Unfortunately, we have not yet been able to accomplish this and will probably have to submit the results for publication based on unadjusted data. No individual patients will be interviewed, charts reviewed, or specimens collected. All work has and will be done with previously established databases.

### CONCLUSIONS

The military beneficiary population appears to be older and have a higher proportion of males and racial minorities compared with the U.S. population. Unadjusted ESRD incidence and prevalence and ESRD etiology in military beneficiaries appears to be similar to the U.S. population. Racial disparity between blacks and whites may be less in the military. ESRD epidemiology in the military can be used to identify needs, design health promotion programs, measure effects of outcomes management programs, and track progress toward meeting kidney goals of *Healthy People 2010* in the MHS.



## DETAIL SUMMARY SHEET

TITLE: Electron Beam Computed Tomography (EBCT) as a Screening Tool in the Pre-Renal Transplant Assessment of Patients with End Stage Renal Disease

KEYWORDS:

PRINCIPAL INVESTIGATOR: LTC Christina M. Yuan MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Nephrology

INITIAL APPROVAL DATE: 16 January 2001

### STUDY OBJECTIVE

To describe the association of EBCT coronary artery calcium score with risk for cardiac events defined by clinical cardiovascular risk assessment (Eagle Score), and cardiac stress test (Dobutamine stress ECHO) in ESRD patients who are candidates for renal transplant, or who are on the transplant list. Secondary objectives are to describe the association of EBCT coronary calcium score with 1) coronary angiographic findings in patients who subsequently receive cardiac catheterization for clinical indications, 2) demographic features (age, sex, race, time on dialysis, hypertension, diabetes) and laboratory values (PTH, homocysteine, CRP, calcium and phosphorus), and 3) occurrence of "hard" coronary events at 1, 2, and 3 years post initial evaluation.

### TECHNICAL APPROACH

150 patients with ESRD ( $\text{CrCl} < 20 \text{ cc min}$ ), who are potential candidates for kidney or kidney-pancreas transplantation and meet the inclusion and exclusion criteria, will be entered. This is a prospective, observational study with cross sectional entry. After baseline collection of laboratory, EKG, and demographic data, all participants will undergo a clinical cardiovascular assessment with Eagle score, and referred for Dobutamine Echocardiogram and EBCT (cardiologist, transplant clinician, and patient are blinded to EBCT). Patient will be assessed, and referred for further work-up by cardiology, as clinically indicated (based on EKG, clinical assessment, and Dobutamine Echocardiogram). Yearly, a history of cardiac events will be elicited by telephone, mail, or in person. Analysis of primary outcome: Association between EBCT and Eagle score/Dobutamine stress ECHO will be examined using analysis of variance and discriminate analysis.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 3 and the total enrolled to date at WRAMC is 11. Three subjects have received transplants. One subject died during induction of anesthesia for a transplant in September of 2002. This was reported to the IRB. This subject had had a normal cardiac evaluation, a normal dobutamine stress ECHO, and a normal EBCT. Autopsy was referred to the DC Coroner's office, which declined the case. Thus, autopsy was not done. Coroner felt death likely "cardiac" in nature. Notably, 4/11 had a EBCT calcium score of "0", suggesting that ESRD patients do not universally have markedly high calcium scores, as has been suggested in the literature. The study is early in its course, and no results are yet available.

### CONCLUSIONS:

None available as yet.

## DETAIL SUMMARY SHEET

TITLE: Acetylcysteine for the Prevention of Contrast Associated Nephropathy in Diabetic Patients Undergoing Coronary Angiography

KEYWORDS: Contrast Associated Nephropathy, Acetylcysteine, Angiography

PRINCIPAL INVESTIGATOR: Robert E. Jeschke, MAJ, MC

ASSOCIATES: A. Simon, LCDR, MC, USNR (PI at NNMC site)

DEPARTMENT: Medicine

STATUS: O

SERVICE: Cardiology

INITIAL APPROVAL DATE: 23 January 2001

### STUDY OBJECTIVE

The primary objective of this study remains the same. The study is designed to determine if acetylcysteine plus hydration is superior to hydration alone for the prevention of contrast-associated renal dysfunction in diabetic patients undergoing coronary angiography. The null hypothesis of this trial is that acetylcysteine will not be superior to standard therapy (hydration) for the prevention of contrast-associated deterioration in renal function.

### TECHNICAL APPROACH

Patients have been and continue to be recruited during pre-cardiac catheterization counseling from the WRAMC Cardiology Service and National Navy Medical Center Cardiology Service on either an inpatient or outpatient basis (please see request for change in protocol memorandum dated 11 September 2001 and NNMC approval letter including NNMC as an additional study site) upon referral for elective cardiac catheterization and selective coronary angiography. Up to 200 patients (all meeting enrollment criteria, male or female) will be enrolled. This study is a randomized, prospective, open-label study comparing the effects of acetylcysteine plus oral hydration versus oral hydration alone in diabetic patients undergoing coronary angiography.

Patients undergo separate randomization at the two study sites, NNMC and WRAMC. Patients are randomly assigned in a 1:1 ratio to one of two arms, standard hydration with the study drug, acetylcysteine, and standard hydration only. All patients receive standard hydration therapy in the following manner: combined oral pre-hydration (1 liter of clear liquids in the ten hours before arrival in the cardiac catheterization laboratory) and intravenous post-hydration (0.45N saline at 300 cc/hr for a total of six hours). Oral fluids will be encouraged after the procedure. Hydration status for patients is followed as indicated on the data collection form monitoring total oral and IV fluids pre and post cardiac catheterization. Patients allocated to the acetylcysteine arm receive standard hydration therapy and 600 mg of acetylcysteine, prescribed by an investigator, orally twice daily beginning on the day prior to contrast exposure and ending on the day of exposure for a total of four doses. Kidney function has been tested by measuring serum creatinine and related variables contained in a standard "Chem 7 or profile 1" noted on the data collection form. These tests are ordered by one of the investigators and measured pre and post angiography. The investigators follow patients within the study period. After the study period the standard follow-up for patients post cardiac catheterization occurs, i.e. the primary angiographer is responsible for follow-up on patients.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study is ongoing with continued enrollment at both WRAMC and NNMC. There have been no adverse events reported since the last APR submitted 13 November 2002.

Acetylcysteine as a possible pre-treatment for reduction in contrast associated nephropathy continues to be subject of ongoing studies and publications. To date, the evaluation of this medication in the high risk diabetic population has yet to be adequately analyzed, thus this study has the potential to contribute to the research already conducted and published in this area.

Work Unit # 01-12001 [*Continued*]

The number of subjects enrolled to the study since last APR (dated 13 November 2001) at WRAMC is 55 and the total enrolled to date at WRAMC is 125. The total number enrolled study-wide is 167 (42 at NNMCC). We will continue to seek an enrollment of 200 patients allowing for evaluation of inter-site variability, post randomization drop outs, and enrollment of 70 usable data points per treatment arm to allow for a significantly powered study.

CONCLUSIONS

This study is ongoing and is very close to completing enrollment. Approval is requested for another year with anticipation of completing enrollment prior to that time.

## DETAIL SUMMARY SHEET

TITLE: Remote Echocardiographic Consults – Diagnostic Concordance – Intra and Inter Consults

KEYWORDS:

PRINCIPAL INVESTIGATOR: Malik, Anwar K., LTC, MC

ASSOCIATES: COL Marina N. Vernalis, MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Cardiology

INITIAL APPROVAL DATE: 5 June 2001

### STUDY OBJECTIVE

To compare diagnostic findings of echocardiograph studies read from VHS tape versus Digital formats.

### TECHNICAL APPROACH

120 ECHO studies have been acquired both digitally and on VHS format at Dewitt Army Community Hospital from July 2000 to June 2001. VHS formats have been read and digital formats have been transferred to WRAMC and are available for interpretation and comparison. We plan to use these studies retrospectively subject to same inclusion/exclusion criteria and methodology as presented in the original protocol.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The total number of patients is 120 whose ECHO data is available for the study in both digital and VHS formats. However, despite exhausting all available resources at Fort Belvoir, we have been unable to locate consent forms for those studies. It appears that we will not be able to find those forms.

### CONCLUSIONS

We regret this major deviation, and request that the HUC permit re-consenting the patients either by mail and/or telephone so that this useful study may be completed, since already a lot of time and treasure has been invested.

## DETAIL SUMMARY SHEET

TITLE: Remote Echocardiographic Consults – Diagnostic Concordance – Intra and Inter Consults

PRINCIPAL INVESTIGATOR: Malik, Anwar K., LTC, MC

ASSOCIATES: COL Marina N. Vernalis, MC, Daniel B. Rayburn Ph.D.

DEPARTMENT: Medicine

STATUS: C

SERVICE: Cardiology

INITIAL APPROVAL DATE: 5 June 2001

### STUDY OBJECTIVE

To compare diagnostic findings of echocardiograph studies read from VHS tape vs. Digital formats.

### TECHNICAL APPROACH

115 ECHO studies have been acquired both digitally and on VHS format at Dewitt Army Community Hospital from July 2000 to June 2001. VHS formats have been read and digital formats have been transferred to WRAMC and are available for interpretation and comparison. We plan to use these studies retrospectively subject to same inclusion/exclusion criteria and methodology as presented in the original protocol.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR is 0 and the total enrolled to date at WRAMC is 0. 115 retrospective studies acquired at Dewitt ACH from July 2000 to June 2001 are being used in the study, as per the approval of addendum dated 9 January 2002. No AEs have occurred since the last APR. No patients have withdrawn since the last APR. A review of recent literature has been performed.

### CONCLUSIONS

In our preliminary assessment, the tele-echo system is noted to be fully capable of acquisition, transmission, and retrieval of digital echo studies without compromising the image quality in an expeditious and confidential fashion.

## DETAIL SUMMARY SHEET

**TITLE:** ARBITER II - **A**Rterial **B**iology for the Investigation of the **T**reatment **E**ffects of **R**educing Cholesterol - A Randomized, Placebo-Controlled, Double-Blind Trial Evaluating the Effect of Long-Acting Niacin on Carotid Intima-Media Thickness

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** Taylor, Allen LTC MC  
**ASSOCIATES:**

**DEPARTMENT:** Medicine  
**SERVICE:** Cardiology

**STATUS:** O  
**INITIAL APPROVAL DATE:** 31 July 2001

### STUDY OBJECTIVE

The purpose of this study is to evaluate the effect of niacin when added to an HMG-CoA reductase inhibitor on carotid atherosclerosis progression.

### TECHNICAL APPROACH

This is a double blind, placebo controlled trial of niacin in the regression of atherosclerosis in patients with known coronary heart disease already treated with a statin. Patients are treated for one year, to the primary endpoint of carotid atherosclerosis assessment utilizing ultrasound measurement of intima-media thickness. There have been no modifications to the technical approach this year.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The study began enrollment in December 2001. To date, 168 patients have been enrolled; 95 since the last APR. An amendment was approved allowing us to identify eligible participants utilizing the Integrated Clinical Database to whom a recruitment invitation was mailed.

The number of subjects enrolled to the study since last APR at WRAMC is 95 and the total enrolled to date at WRAMC is 168. The study is approved to enroll up to 200 subjects. The required sample size is 140. The number of patients who have fully completed the 12-month study period is 63. The number of patients who have withdrawn consent to continue in the study is 11 (93% retention rate). Adverse effects have been reported in eight subjects during the past year. The total number of AE reports is eight. One serious adverse event occurred involving death of a woman participant. Study medication had been withdrawn early in the study due to rash (as reported in the 2002 APR). Months later she experienced a pulmonary embolism, and later died at home. This event was considered to be unrelated to the study medication (she had been off study medication for approximately six months). The study medication has been well tolerated. Other than occasional flushing (as noted in the consent form), we have not noted any severe abnormalities in laboratory monitoring requiring discontinuation of the study medication.

There is no recent literature that examines the incremental value of niacin added to statin for either the prevention of cardiovascular events or intermediate endpoints. Thus, the study hypothesis remains valid. Interim reports have continued to highlight the safety of this combination therapy, mirroring our experience thus far.

### CONCLUSIONS

Enrollment in ARBITER 2 has proceeded well and we have surpassed our required sample size. Retention in the study is at an acceptable level. Serious adverse events are uncommon in this high risk, coronary heart disease population. We anticipate discontinuing active enrollment soon, and continuing to focus on retention and completion of the 12 month study period.

## DETAIL SUMMARY SHEET

**TITLE:** A Comparison of the Effects of Rosiglitazone and Metformin on Markers of Inflammation and Carotid Plaque Burden in Patients with Type 2 Diabetes Mellitus. Cardiovascular Effects of Hypoglycemic Medication in Diabetes – CHD Study

**PRINCIPAL INVESTIGATOR:** MAJ Derek J. Stocker MC

**ASSOCIATES:** Taylor, Vigersky, Langley

**DEPARTMENT:** Medicine

**SERVICE:** Endocrine

**STATUS:** O

**INITIAL APPROVAL DATE:** 23 January 2001

### STUDY OBJECTIVE

Primary objective: Does rosiglitazone have an anti-inflammatory effect compared to metformin, measured as a decrease in certain markers of inflammation, particularly C-reactive protein? Secondary objective: Does rosiglitazone have an anti-atherosclerotic effect compared to metformin, measured as a decrease in carotid plaque burden?

### TECHNICAL APPROACH

We are enrolling poorly controlled type 2 diabetics in a study of two FDA-approved medications, rosiglitazone and metformin. Patients are randomly assigned to one of these medications in an open-label study and followed for six months. Over this period, serial carotid intimal thicknesses (CITs) are obtained to assess for changes in atherosclerosis and serial labs are drawn to check for the anti-inflammatory effects of each of these medications. We have added a sub-study to evaluate the nature of weight gain and body composition changes on these medications with the use of DEXA scans every three months on the study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The 60<sup>th</sup> patient completed the study this month, at which point we have begun to perform interim analysis. Dr. Taylor is in the process of interpreting the CITs for the completed patients and the frozen serum will be submitted to the lab for batched analysis of CRPs during the first week in December 2002. A total of 78 patients have been enrolled in the study, of which 19 have withdrawn. There were no unexpected adverse reactions and the vast majority of subjects have improved their glycemic control on therapy. Five patients withdrew due to adverse GI effects on Metformin; two patients withdrew due to edema on Rosiglitazone; one patient experienced weakness on Rosiglitazone and asked to stop; one elderly gentleman experienced a traumatic hip fracture shortly after starting Rosiglitazone and withdrew due to inability to follow-up; four patients were screened, enrolled, and randomized to treatment, but were noted to have disqualifying lab values and were never started on therapy; one patient was unexpectedly transferred away during the course of the study; two patients stopped after the first visit for personal reasons; and three patients attended the first five visits, but failed to return for the sixth and final appointment. Since the last APR, we have added a sub-study of patients enrolled since MAR 02 using DEXA scans to determine the nature of body composition changes in patients on Rosiglitazone compared to Metformin. No conclusions to date. There has been little published data since the last APR comparing these medications. One abstract by Masateru Ohnaka and Tatsuaki Murakami at the AHA national meeting in NOV 2002 concluded that thiazolidinediones compared to placebo demonstrated an improvement in CIT at one year. Numerous studies have demonstrated the new appreciation of CRP as a significant risk factor for coronary artery disease and atherosclerosis, most significantly: Ridker PM, Rifai N, Rose L, Buring JE, Cook NR. Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. (N Engl J Med. 2002 Nov 14;347(20):1557-65.) The number of subjects enrolled to the study since last APR at WRAMC is 66 and the total enrolled to date at WRAMC is 78.

CONCLUSIONS None.

## DETAIL SUMMARY SHEET

TITLE: Using Telemedicine and Wireless Technology to Improve Diabetic Outcomes in Poorly Controlled Patients

KEYWORDS: Diabetes Mellitus, Telemedicine

PRINCIPAL INVESTIGATOR: Vigersky, Robert A. COL MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Endocrine

INITIAL APPROVAL DATE: 20 March 2001

STUDY OBJECTIVE: Determine whether or not patients who are given one of three different technologies to communicate their home blood sugar results to their provider have better glycemic control than those who get "routine" Diabetes Institute care.

### TECHNICAL APPROACH

STANDARD CARE: Group 1.

All patients will receive standard Diabetes Institute care. During the patient's initial visit, a comprehensive medical history will be taken to confirm the diagnosis, review and reassess the previous treatment, evaluate past and present degrees of glycemic control, determine the presence or absence of chronic complications of diabetes, assist in formulating a management plan, and provide a basis for continuing care. A physical examination will be performed during the initial evaluation. Each patient will undergo any routine laboratory tests as deemed appropriate by the health care provider. A diabetes management plan will be formulated as an individualized therapeutic alliance among the patient and family, the provider, and other members of the health care team skilled in diabetes management.

RESEARCH: Group 2, 3, and 4.

After obtaining baseline laboratory data, eligible patients will be randomized to one of three intervention groups using a computerized random number generator program. Patients assigned to Group 2 (the first intervention group) will transmit their glucose measures through a modem compatible to their glucometer to a specially designed secure website. Group 3, the second intervention group, will consist of patients who will transmit their glucose measures via WebTV to the same specially designed website. Group 4, the third intervention group, will consist of patients who will transmit their glucose measurements via their Internet accessible computer to the same specially designed website. Patients who transmit their glucose measures through a modem will not be able to view graphical or tabular representations of their data. Patients who transmit their glucose measures using a WebTV device or personal computer will be able to view graphical or tabular representations of their data. Patients in Group 2, 3, and 4 will transmit their glucose data using 128-bit encryption technology to their health care provider weekly. Nurse practitioners will review these data weekly and intervene personally with the patient whenever it is clinically appropriate. All research groups will also receive standard Diabetes Institute care as outlined above for Group 1.

Patients in an intervention group (Group 2, 3, or 4) will receive training to support the technology assigned to their group. The project officer to each participant at the medical treatment facility will administer training where he/she usually receives diabetes care. The patient training modules will include specially developed educational materials manuals and videotaped instruction (not to exceed thirty minutes). Patients will schedule appointments for training with the project officer.

Identifying patients will protect patient confidentiality by a unique serial number on their glucometer, regardless of the technology used. Only the treating nurse practitioners and Principal and Associate Investigators will know this number and the patient's identifying information. Patients who transmit data to the secured WRAMC website via modem will utilize a TCP/IP connection. Patients who transmit using a WebTV device will access the



secure WRAMC website via an HTTP connection. Displayed responses will be limited to historical data and the patient's first name. Patients who transmit data using a personal computer will also access the secure WRAMC website using an HTTP connection. Displayed responses will be limited to historical data and the patient's first name. Risks to patients are only that of potential breach of confidentiality. In no case will patient identifiers will be included in an electronic transmission. The Principal Investigator will keep the complete list in a secure file at WRAMC. The WRAMC diabetes database will serve as the central repository for all data from this study. Data collected by Health Sentry will be available to the Principal and Associate Investigators in real time via secure encryption technology. The data remains on the Health Sentry server to allow for historical trends to be clinically evaluated. Patients will have access to their own data on the Health Sentry server.

**TECHNOLOGY:** The software development and maintenance and the establishment of a secure website will be performed under contract by Health Sentry, who will modify a previously developed proprietary product for the investigators. This unique software allows the patient to use any brand of glucose meter to download their data into a secure website. Patients will not be required to execute any paperwork for the technology contractor that might reveal their identity beyond the glucometer serial number. The patients will enter the website through the WRAMC website. The data will be automatically analyzed and displayed in both numeric and graphic formats. All Principal and Associate Investigators will have continued free and open access to the secured patient data. Health Sentry will also produce a patient training module that will include manuals, user's guides, and videotapes. These specially developed educational materials will be owned by WRAMC and maintained on the facility. Participating patients will not be permitted to retain the technology instrument (modem, WebTV device, or computer cable) provided them by Health Sentry after completion of this study. Health Sentry will maintain an 800 number hotline for support. The only patient data resident in the Health Sentry database will be the patient's glucometer serial number and blood glucose levels.

Group 2: Health Sentry (the contractor) will provide the following support for the glucometer:

Fifty patients will receive a modem, and then be assigned a unique participant identifier (their glucometer serial number). The study participants will communicate their glucose measures using a standard telephone line to the Diabetes Institute health care provider weekly. The modem will be pre-customized by Health Sentry to dial a toll free phone number to the contractor's server. Software to migrate this information into the common database using a secure website. Equipment provided to participants by the contractor will have no usefulness following the conclusion of the study and discontinuation of the specially developed study website.

Group 3: Health Sentry will provide the following to support WebTV use:

Fifty patients will receive a WebTV control device and WebTV keyboard to upload their glucometer measurements. The WebTV controller devices will interface with the patient's glucometer and deliver these readings using an infrared beam to the WebTV appliance. These data will be transmitted directly to the Health Sentry server. No Health Sentry employee or affiliate, nor will any individual, institution or organization outside of the WRAMC Diabetes Institute have access to any patient demographic data. The contractor will not analyze or otherwise dispose of patient data. The contractor will store anonymized patient data distribution to investigators. Patients will be identified by meter serial number only. Software to migrate this information into the common database is to be integrated into the WRAMC website. Equipment provided to participants by the contractors will have no usefulness following the conclusion of the study and discontinuation of the specially developed study website.

Group 4: Health Sentry will provide the following to support PC use:

Fifty compatible computer cable links to allow patients to upload their glucometer measures using their own Internet capable PCs. These data will be transmitted directly to the Health Sentry server. The contractor will not analyze or otherwise dispose of patient data. The contractor will store anonymized patient data for distribution to PIs. Software to migrate this information into the common database is to be integrated into the WRAMC website. Equipment provided to participants by the contractors will have no usefulness following the conclusion of the study and discontinuation of the specially developed study website.

Addendum Technology:

The Diabetes Management and Communication System (DMCS) will integrate a glucometer (Accu-Chek Advantage) with a wireless enabled PDA (the Compaq iPAQ). The iPAQ provides the capability to assist the patient's management of his/her disease through the development of an application that calculates the amount of insulin to be given at any time ("bolus computation"). This calculation may incorporate several parameters including the ambient blood glucose level, the carbohydrates (carb) content of the meal, and an adjustment for exercise. These parameters are already being incorporated into the patient's regimen, but on a manual basis. The device will also track compliance in testing blood sugars and in taking other medications. FIPS 140-1 compliant cryptography will be enabled on the device.

**PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE:** One hundred twenty-three patients have been entered on the main study. The preliminary results on the first 73 patients show that after six months, the group that was given the technology (n=46) improved their mean  $\pm$  s.d. % Alc from 10.03%  $\pm$  2.59 to 7.68%  $\pm$  1.86 while the control group (n=27) improved from 10.3%  $\pm$  2.27 to 8.76%  $\pm$  2.24. Analysis as to which of the technologies produced the best results is deferred until more patients complete the study.

There have been no serious adverse events to date. The protocol was modified in March of 2002 by adding a wireless Diabetes Management and Communication System (DMCS) whose technical details are listed above. The addendum adds 24 patients with Type 1 diabetes mellitus who will be given an opportunity to use a newly developed wireless technology – the Diabetes Management and Communication System (DMCS) – to communicate blood sugars and other information to their providers. They will be between 18-70 years of age, currently using insulin pumps, and have an HbA1C greater than 7% and/or frequent hypoglycemic events ( $> 2$  per week). Exclusion and discontinuation criteria are unchanged except patients will be Type 1 diabetics using an insulin pump and must have access to a computer connected to the Internet. Subjects will be recruited by the Diabetes Institute providers who manage most patients in the Walter Reed Health Care System that use insulin pumps. They will not be compensated for their participation. They will be randomized into a DCMS group and a control group. Following a six-month period, the patients will cross over to the other group and the analysis will be conducted on the entire trial population. The DMCS group will transmit their data daily. Their data will be analyzed and the results/recommendations communicated by phone at least once weekly by the Project Officer or their Diabetes Institute provider. The patients' diabetes care will continue to be provided by their same Diabetes Institute provider using the same practice guidelines of the Diabetes Institute.

The milestones for this addendum are as follows:

- Receipt of \$175,000 P-8 funding in February 2002
- Creation of a Statement of Work for the HealthSentry contractor
- Purchase of 10 iPAQs and wireless cards
- Programming the iPAQ with the parameters to be entered and tracked i.e. insulin dose, carbohydrate count, exercise, and medication usage, in addition to the blood sugar
- Modification of the HealthSentry web site to accept data other than blood sugar, i.e. insulin dose, carbohydrate count, exercise, and medication usage
- Procurement complimentary copies of a caloric/carbohydrate counter program – CalorieKing – for inclusion into the iPAQ

Patient recruiting will begin on 6 January 2003. The protocol was also modified on 8 November 2002 by the addition of two associate investigators. The number of subjects enrolled to study since last APR is 136. The total enrolled to date at WRAMC is 136.

**CONCLUSIONS:** The use of telemedical technology appears to have substantially benefited those patients who used it by reducing their hemoglobin A1cs more than that of the control group. Patient recruitment continues for the main study, and will begin in January 2003 for the addendum.

## DETAIL SUMMARY SHEET

**TITLE:** The Avandia Worldwide Awareness Registry (AWARe): Comparison of Avandia and Actos in “Real World” Medical Practice

**KEYWORDS:** Diabetes Mellitus. Avandia, Actos, Rosiglitazone, Pioglitazone

**PRINCIPAL INVESTIGATOR:** Vigersky, Robert A. COL MC  
**ASSOCIATES:**

**DEPARTMENT:** Medicine  
**SERVICE:** Endocrine

**STATUS:** O  
**INITIAL APPROVAL DATE:** 27 March 2001

### STUDY OBJECTIVE

The objective of this study is to determine:

1. Whether thiazolidinedione (TSD) class of antidiabetic pharmaceutical agents has beneficial effects on cardiovascular risk factors (e.g. lipids, blood pressure, and proteinuria).
2. The safety and compliance with antidiabetic drug therapy in a population of patients with Diabetes Mellitus Type 2.
3. In a “real world” treatment setting whether rosiglitazone or pioglitazone provide sustainable glycemic control in the long term (6 months-1 year).
4. The impact of antidiabetic drug therapy on patient’s health-related quality of life and satisfaction with treatment.
5. Whether differences exist between the two currently available drugs in the thiazolidinedione class, Avandia and Actos, in Objectives 1-5.

### TECHNICAL APPROACH

This is a combination of an observational and a randomized control trial. The observational aspect is standard of care for the Diabetes Institute. It involves the monitoring of patients’ data who are treated with a sulfonylurea and/or a TZD and/or metformin and who are not placed on a TZD during the duration of the study. The interventional aspect is the randomization of patients who require a TZD to either rosiglitazone or pioglitazone. As a part of the research, demographic and clinical data on enrolled patients will be entered into the Avandia Worldwide Awareness Registry (AWARe).

### PRIOR AND CURRENT PROGRESS

The number of subjects enrolled to the study since last APR at WRAMC is 276 and the total enrolled to date at WRAMC is 276. The total number enrolled study-wide approximately 1500.

Accrual of patients into the observation arm of the study continues at a steady pace. A total of 276 patients have been registered to date. There are only a small number of patients who are enrolled into the interventional arm of the study (n=9). There has been no data analysis to date. There have been no serious adverse events related to the study. An addendum submitted in February 2002 permitted retrospective tracking of patients’ data. Thus, at present, patients will be tracked prospectively for a minimum of one year after study enrollment, and tracked retrospectively for up to five years prior to study enrollment. Retrospective data will be collected at approximately three-month intervals. Retrospective data will be collected to extend the duration and number of observations to ensure accurate recognition of trends, disease severity, and disease management.

### CONCLUSIONS

Patients continue to be entered into the AWARe study’s observational and intervention arms.

## DETAIL SUMMARY SHEET

TITLE: Pilot Study - Recombinant TSH Stimulation of Radioactive Iodine Uptake in Hyperthyroidism

KEYWORDS: Thyroid, Thyrotoxicosis, Thyrogen

PRINCIPAL INVESTIGATOR: Bernet, Victor LTC MC

ASSOCIATES: Dr. Aaron Stack, Dr. Thomas Allen, and Dr. Henry Burch.

DEPARTMENT: Medicine

STATUS: O

SERVICE: Endocrinology

INITIAL APPROVAL DATE: 15 May 2001

### STUDY OBJECTIVE

- 1) Determine the effect of rhTSH on RAIU in patients with hyperthyroidism, specifically those cases with only minimally abnormal RAIU levels.
- 2) Assess the response of patient symptoms as well as Free T4 and Free T3 levels in hyperthyroid patients receiving rhTSH in combination with RAIU or with <sup>131</sup>I treatment.
- 3) Evaluate the number of patient's achieving euthyroidism or hypothyroidism within six months status <sup>131</sup>I treatment in conjunction with rhTSH.

### TECHNICAL APPROACH

We propose a two-phase study consisting of a total of ten patients with hyperthyroidism with radioactive iodine uptakes (RAIUs) of 15 to 30%. Entry into the study would be limited to those patients who have undergone evaluation by an endocrinologist and have been found to have primary hyperthyroidism as evidenced by history, physical examination, thyroid blood tests (TSH, free T4 and/or free T3) plus standard CBC and Chem 20 panel. The TSH level would need to be suppressed to  $\leq 0.3$  mIU/L, where as the Free T4 and Free T3 would range between the upper normal to mildly elevated beyond the normal range (but no higher than a Free T4  $> 40$  pmol/L, Free T3  $> 8.5$  pmol/L), consistent with autonomous thyroid function. A 99m-technetium thyroid scan and 24 hour RAIU are to have been completed within 30 days prior to entrance into study, and must confirm the presence of autonomous (overactive) thyroid tissue. Participation will require the finding of a 24-hour RAIU between 15 to 30%. Patients will be offered the standard range of therapies to include: antithyroidal medication (propylthiouracil or methimazole), surgery, or <sup>131</sup>I as appropriate for their form of hyperthyroidism. In summary, those patients meeting inclusion and exclusion criteria, and who have chosen <sup>131</sup>I therapy, after careful discussion of therapeutic options with their endocrinologist, will be offered entry into the study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Presently, we have been able to recruit only one patient. Two issues appear to play a role in the difficulty in patient recruitment. One is the amount of follow-up visits required with the study. Several patients felt they could not find the time to participate. Secondly, our conservative exclusion criteria appear to significantly reduce the number of patients eligible for the study. Our team may need to reassess if such stringent exclusion criteria are really indicated - especially the fairly young age cut off. No new scientific literature has been published which would indicate that either the study would be unsafe or that a change in methods is required. The one patient had no adverse reaction to any of the Thyrogen injections and tolerated the study intervention well. The number of subjects enrolled to the study since last APR at WRAMC is 1 and the total enrolled to date at WRAMC is 1.

### CONCLUSIONS

None. Continue with attempts to enroll patients as planned.

## DETAIL SUMMARY SHEET

TITLE: Determination of Thyroid Nodule Malignancy with 18F-FDG Coincidence Imaging and Tc-99m Depreotide Scintigraphy

KEYWORDS:

PRINCIPAL INVESTIGATOR: Langley, Roy W. MAJ MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Endocrine

STATUS: O  
INITIAL APPROVAL DATE: 19 June 2001

### STUDY OBJECTIVE

The objective of this study is to determine if non-invasive imaging using 18F-FDG and Tc-99m Depreotide can determine thyroid nodule malignancy and how this compares to FNA.

### TECHNICAL APPROACH

Subjects with thyroid nodules awaiting thyroidectomy are imaged using 18F-FDG Coincidence Imaging and Tc-99m Depreotide Scintigraphy. The results are compared with the cytology from FNA and the histology from thyroidectomy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Twenty subjects have been enrolled to date. Histologically confirmed papillary or follicular carcinomas were found in 6 subjects (5 with PTC only, 1 with FTC only, and 1 with both FTC and PTC). One subject has a follicular adenoma (toxic nodule). This represents an additional 9 subjects enrolled since the submission of last year's progress report. There are no benefits to subjects from this study.

Due to production problems with depreotide, there have been no available supplies since the beginning of this year. It is not clear when depreotide will be available, but it is expected before the end of this year. There will be no further enrollments until depreotide is again available.

Review of the literature found a retrospective report (Van Den Bruel A, JCEM 87(4):1517-20) on incidental thyroid lesions on PET imaging with 18-FDG, suggesting a high malignancy rate. A recent article (Kresnik E, Surgery 133(3):294-9) discusses PET imaging with 18-FDG in 43 thyroid nodules prior to thyroidectomy. The results suggest that carcinomas may be distinguished from non-adenomatous nodules and most but not all subtypes of adenoma. No article referencing depreotide imaging and thyroid nodules were found.

### CONCLUSIONS

The sample size to date is too small for meaningful results. Further recruitment is pending the availability of depreotide. Additional publications in the literature suggest that 18-FDG PET imaging can be helpful in evaluating the malignant potential of thyroid nodules. However, further research is required to clarify its appropriate role.

## DETAIL SUMMARY SHEET

TITLE: Association of Helicobacter pylori Infection with Coronary Heart Disease Detected by Electron Beam CT

KEYWORDS:

PRINCIPAL INVESTIGATOR: Duncan, Marten CPT MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Gastroenterology

INITIAL APPROVAL DATE: 9 January 2001

### STUDY OBJECTIVE

To determine if an association between Helicobacter pylori infection and coronary heart disease exists.

### TECHNICAL APPROACH

The associate investigator (AI) from the Department of Radiology will provide two lists of patients who have presented to the WRAMC EBCT for routine examinations and are potential participants in the study. One will be of patients with zero calcium score (controls), the other of patients with a high calcium score >300 (cases).

1. Letters will be mailed to all patients inviting them to participate in our study. One month after the first letter, a second letter will be mailed to those patients that did not respond to the first letter. One month after the second letter was mailed, a third letter will be sent. A maximum of three letters will be mailed. One month after the third letter, we will prospectively enroll patients until our goal of 214 patients in each group is reached.
2. Enrolled patients will answer a questionnaire. This will include questions of demographic data such as age, race, rank, and education (as a measure of socioeconomic status).
3. Phlebotomy of 21 cc will be performed on all enrolled patients.
4. Serum of 14 cc will be used to test for H. pylori IgG, CRP, Lipid profile, Fibrinogen and Chlamydia pneumonia.
5. Serum of 7 cc of blood will be frozen and stored at the GI lab in USUHS until completion of the study (one year). Patients that test positive for H. pylori IgG will have CAG-A tested on these frozen samples. CAG-A testing will be performed using an ELISA at the laboratory of Dr. Andre Dubois. The identity of the patients will not be on the samples and will only have a coded number. Patients may ask that their serum be withdrawn at any time. Patients that test positive will be notified of this result.
6. Frozen serum will be destroyed at the completion of the study. There will be no human genetic studies performed on the sera. There have been no modifications to the methodology.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The total number of subjects enrolled to date at WRAMC is 100. There are no adverse events to report. A recent review of the literature showed twelve studies within the last eighteen months. The studies still contradict one another as to the role of H. pylori in the pathogenesis of atherosclerotic coronary artery disease (ASCAD). Further prospective information would be valuable in helping to determine the role, if any, that H. pylori has on ASCAD.

### CONCLUSIONS

No conclusion can be drawn at this time.

## DETAIL SUMMARY SHEET

**TITLE:** An Efficacy and Safety Study of Intravenous Pantoprazole in the Prevention of Recurrent Peptic Ulcer Bleeding After Successful Hemostasis (Sponsored Study by Wyeth-Ayerst Research)

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** Baroni, Darren S. MAJ MC  
**ASSOCIATES:**

**DEPARTMENT:** Medicine  
**SERVICE:** Gastroenterology

**STATUS:** C  
**INITIAL APPROVAL DATE:** 17 April 2001

### STUDY OBJECTIVE

To evaluate the efficacy and safety of intravenous pantoprazole in the prevention of re-bleeding in patients with bleeding peptic ulcer disease after successful endoscopic hemostatic therapy. This study will compare the mortality rate, units of blood transfused after endoscopy, length of hospital stay, length of intensive care unit (ICU) stay, and the need for urgent intervention between treatment groups.

### TECHNICAL APPROACH

Patients presenting to the WRAMC ER with an upper GI bleed will be screened as potential candidate for this study. The on-call GI fellow will contact the PI when a patient presents with signs and/or symptoms consistent with a GI bleed. All GI staff and fellows will be familiarized with this study for screening and baseline evaluation. When all inclusion and exclusion criteria have been considered and the patient demonstrates bleeding source from a peptic ulcer and the patient is eligible to continue in the study, random administration of intravenous test article (IV Protonix or IV Zantac) will start within two hours of endoscopy and successful hemostasis. The PI will perform the baseline ophthalmology exam. The day 4 post-infusion eye exam will be performed by a staff from the Department of Ophthalmology. The patient will remain in the ICU or, when medically stable, be transferred to the medical ward during the 72-hour infusion.

### PRIOR AND CURRENT PROGRESS

The number of subjects enrolled to the study since last APR at WRAMC is 0. The total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 161.

There are no new literature or findings obtained thus far. There are no new amendments or modifications to the research study since the last review. There were a total of 25 adverse events reported in all multi-center sites. There were no adverse events reported at WRAMC.

### CONCLUSIONS

There are no conclusions at this time.

## DETAIL SUMMARY SHEET

**TITLE:** Effect of Complete Intraesophageal Acid Ablation Upon Cellular Markers of Proliferation, Differentiation, and Apoptosis in Long-Segment Barrett's Esophagus

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** Napierkowski, John MAJ MC

**ASSOCIATES:** Dunaway, Peter MAJ MC, Wong, Roy KH COL MC, Maydonovitch, Corinne

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Gastroenterology

**INITIAL APPROVAL DATE:** 24 April 2001

### STUDY OBJECTIVE

To determine the effect of intraesophageal acid ablation upon cellular markers of proliferation and differentiation in specialized intestinal metaplasia.

### TECHNICAL APPROACH

Subjects with diagnosis of LSBE will be invited to participate in the study. These subjects will be on some form of anti-secretory therapy as routine therapy for BE. To determine the degree of acid reflux, subjects will first have an esophageal manometry performed followed by a 24 hr pH study. The following day, the subjects will undergo an esophagogastroduodenoscopy examination (EGD) where 4 jumbo biopsy samples will be taken from each of the six sites specified as per the protocol. Two sets of biopsies will be shipped to Dr. Jeffrey Lee, who will perform the COX-2 and PCNA staining. Another set of biopsies will be kept in 10% formalin for DNA flow cytometry at a future date. The final set will be stored in a -70° C freezer for quantitative COX-2 mRNA DNA flow cytometry at a future date. Several of these stored samples have been sent to an outside lab (Mayo Clinic) for further studies of markers of proliferation. Remaining stored samples will be analyzed within 5 years or will be discarded. Subjects will then have their anti-secretory discontinued for 2 weeks, but will be allowed to take over the counter antacids. They will then undergo a repeat 24 hr pH study to quantify the degree of acid reflux into the esophagus. A second EGD with a similar distribution of jumbo biopsies will be performed and the same histologic and immunohistochemical analyses will be performed. The biopsies will be distributed, shipped, and analyzed in a similar manner. Subjects will then be put on high dose acid suppression with Rabeprazole (40 mg BID/TID) plus ranitidine (150 mg QHS), for two weeks and subjects will then undergo a final 24 hr pH study for adequacy of ablation, and final EGD with biopsies exactly like that mentioned above. The biopsies will be distributed, shipped, and analyzed in a similar manner. Changes in histology and immunohistochemistry will then be compared within and between the three treatment regiment groups (clinical PPI therapy, off therapy, and total acid ablation). A two-page symptom related questionnaire will be given to the patient prior to each 24-hr pH study. This will be returned the following day when the patient presents for the EGD.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been no recent literature that would alter or amend the research study. The number of subjects enrolled to the study since last APR at WRAMC is 9 and the total enrolled to date at WRAMC is 17.

### CONCLUSIONS

The study is ongoing. Preliminary data show a trend toward decreased COX2 expression in Barrett's epithelium, and a decrease in Ki67 expression in squamous tissue with esophageal acid normalization.



## DETAIL SUMMARY SHEET

TITLE: The Timing of Liver Enzyme Elevation and Hepatitis C Seroconversion in a Cohort of United States Military Gulf War Veterans

KEYWORDS:

PRINCIPAL INVESTIGATOR: COL Kent C. Holtzmuller MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Gastroenterology

STATUS: C  
INITIAL APPROVAL DATE: 1 May 2001

### STUDY OBJECTIVE

To determine the rate of HCV and presence of abnormal liver enzymes in serum samples banked in the DOD Serum repository prior to the Persian Gulf War (PGW) in subjects found to have hepatitis C or elevated serum enzymes following the PGW.

### TECHNICAL APPROACH

CCEP and AFIP databases were utilized to identify subjects who were hepatitis C positive or who had elevated liver enzymes following the PGW. These subjects were cross-referenced with serum samples banked prior to the PGW at the DOD serum repository. The HCV samples obtained are being assessed for hepatitis C. The ALT is being assessed on the samples obtained from the abnormal ALT patients. There has been no change in the methodology of the protocol as written.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no recent publications in the literature related to this field.

The number of subjects enrolled to the study since last APR at WRAMC is 62 and the total enrolled to date at WRAMC is 62.

### CONCLUSIONS

58/62 Gulf War Veterans (GWVs) found to have hepatitis C (HCV) following the Gulf War were discovered to have HCV antibodies on pre Gulf war serum samples. The four GWVs that did not have antibodies on pre deployment serum were not HCV RNA positive on post Gulf War serum.

GWVs did not contract HCV during the Persian Gulf War.

(Manuscript is in preparation.)

## DETAIL SUMMARY SHEET

TITLE: Tele-Hepatitis Phase I - Validation of Desktop Video Teleconferencing for Evaluation of Patients with Hepatitis C

KEYWORDS:

PRINCIPAL INVESTIGATOR: COL Kent C. Holtzmuller MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Gastroenterology

STATUS: O  
INITIAL APPROVAL DATE: 29 May 2001

### STUDY OBJECTIVE

To determine the concordance of visual physical exam findings between exams performed via desktop Video Teleconferencing (VTC) and in person, face-to-face exams.

### TECHNICAL APPROACH

There have been no changes to the protocol. Direct face-to-face exams will be performed by a physician and then compared to a different physician's exam performed via VTC. There have been no modifications.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have no publications related to Telemedicine and liver disease.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is \_\_\_\_\_.

### CONCLUSIONS:

None.

## DETAIL SUMMARY SHEET

TITLE: B-Catenin Mutations and Nuclear Accumulation are Early Events in Hepatic Carcinogenesis:  
Role as a Marker to Determine Risk for Hepatocellular Carcinoma in Hepatitis B Patients

KEYWORDS:

PRINCIPAL INVESTIGATOR: Holtzmuller, Kent, COL, MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Gastroenterology

STATUS: O  
INITIAL APPROVAL DATE: 12 June 2001

### STUDY OBJECTIVE

1. To establish the prevalence of  $\beta$ -catenin nuclear localization and mutation in subjects with hepatocellular carcinoma and in subjects with chronic viral hepatitis.
2. To observe if the presence of such  $\beta$ -catenin mutations may be used as a biomarker for future HCC development in subjects with cirrhosis due to chronic viral infection.

### TECHNICAL APPROACH

The liver biopsy procedure log books in the Gastroenterology Clinic, WRAMC, are being reviewed to identify patients who have undergone liver biopsy for the diagnoses of hepatitis C, hepatitis B, and hepatocellular carcinoma beginning in May 1991. The pathology report and liver tissue block will be identified. Four 4 um and two 50 um tissue sections will be obtained from the tissue block. The tissue slides will be coded by a unique identifier. Subjects will not be identified by name or SSN. The coded tissue will be sent to NIH for the  $\beta$ -catenin studies.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The liver biopsy procedure log book is currently being reviewed to find patients who meet the diagnostic criteria for entry into the study. However, patients and their tissue blocks have not been selected to date. Patients will be selected some time in the next four months. The tissue blocks will then be reviewed to determine if adequate liver tissue is available to be included in the study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

None to date.

## DETAIL SUMMARY SHEET

TITLE: CALGB 59906 - A Phase II Study of Sequential Doxorubicin and Topotecan in Relapsed or Refractory Intermediated or High-Grade Non-Hodgkin's Lymphoma

KEYWORDS: Hodgkin's disease, chemotherapy, cycles, relapsed

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 21 November 2000

### STUDY OBJECTIVE

To evaluate the response rate and time-to-progression or failure in patients with relapsed or refractory intermediate- or high-grade NHL to the combination of sequential doxorubicin/topotecan. To evaluate the toxicity of sequential doxorubicin/topotecan in patients with relapsed or refractory intermediate- or high-grade NHL.

### TECHNICAL APPROACH

Patients will be treated for a maximum of six cycles. Each cycle will consist of 21 days. Patients will receive doxorubicin IVP on day 1 and topotecan IV on days 3, 4, and 5. Treatment will be for a minimum of two cycles in the absence of intolerable toxicity or clear progression of disease.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 14, if multi-site study. No toxicities reported.

Ref: Jun 02 CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 59804 - A Phase I/II Study of Gemcitabine/Vinorelbine/Liposomal Doxorubicin in Relapsed/Refractory Hodgkin's Diseases

KEYWORDS: Hodgkin's disease, chemotherapy, relapse

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 30 November 2000

### STUDY OBJECTIVE

To evaluate the toxicity of four dose levels of Gemcitabine, Navelbine, and Doxil (GND) in patients with relapsed Hodgkin's disease. To determine the complete and partial response rates of relapsed Hodgkin's disease to the combination of GND.

### TECHNICAL APPROACH

Patients will be registered to one of four gemcitabine/Navelbine/Doxil (GND) dose levels. There will be no inpatient dose escalations. Patients will receive a maximum of six cycles, each cycle consisting of 21 days. The chemotherapy will be given on days 1 and 8 of each cycle, intravenously. Restaging will occur every two cycles. Non-responding patients will be removed from therapy after two cycles.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 3 and the total enrolled to date at WRAMC is 6. The total number enrolled study-wide is 47, if multi-site study. Grade 4 toxicities include 9 neutrophils/granulocytes.

Ref: Jun 02 CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 59901 - A Phase II Study of 506U78 in Patients with Previously Systemically Untreated Cutaneous T-Cell Lymphoma or With Refractory or Relapsed Non-Cutaneous Peripheral T-Cell Lymphoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Joseph Drabick COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 12 December 2000

### STUDY OBJECTIVE

This study has two objectives. 1. To determine the complete and partial remission rates, as well as the remission duration, in patients with previously systemically untreated cutaneous T-cell lymphoma (CTCL) or with refractory or relapsed non-cutaneous peripheral T-cell lymphoma (PTCL) receiving 506U78 (1.5 gm/m<sup>2</sup>/day) on an alternate day schedule (days 1, 3, 5). 2. To determine the safety and toxicity associated with 506U78 administered on this schedule to these patients.

### TECHNICAL APPROACH

Eligible patients will receive study drug, 506U78, as a 2 hour IV infusion at a dose of 1.5g per m<sup>2</sup> on Monday, Wednesday and Friday (days 1,3,5) every 21 days until disease progression, complete response, or development of unacceptable toxicity. Renal function will be closely monitored and treatment will be modified if necessary. A physical exam, lab-work, and toxicity assessment will be done before each cycle. A weekly CBC will be done with dose modification, if necessary. Restaging studies will be done after every two cycles to assess for response to treatment. Careful assessment for neurological toxicity will be continuous and treatment will be stopped if this toxicity occurs.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study is still in the process of accruing patients at this time, so there are no publications reporting data at this time.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 11, if multi-site study. No Grade 4 toxicities reported. There were no adverse events reported here at WRAMC, but all institutes using the compound 506U78, IND52611 received two safety reports (AE #1805378 dated 8 April 2002 and AE #1971856 dated 29 April 2002).

Ref: CALGB June 2002 Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 79804 - Issues of Survivorship Among Breast Cancer Survivors

KEYWORDS:

PRINCIPAL INVESTIGATOR: Joseph J. Drabick COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 27 February 2001

### STUDY OBJECTIVE

1. To determine the prevalence of physical, economic, psychosocial and spiritual consequences of survivorship, including issues related to reproduction, menopause, osteoporosis, post-mastectomy/lumpectomy pain, and lymphedema among a cohort of disease-free long-term breast cancer survivors.
2. To determine how these problems affect overall health related quality of life (HRQL).

### TECHNICAL APPROACH

Potentially eligible patients were identified by research personnel at Wake Forest University School of Medicine (WFUSM) and by research personnel at WRAMC. An introductory letter was sent to potential patients. About one week after the letters were sent, the patients were contacted by phone by research personnel from WRAMC to further explain the study, answer questions, assess interest in participation in the study, and arrange for a follow-up appointment at WRAMC to complete the consent process. After registration to the study, a professional research interviewer from WFUSM will send a questionnaire to the patient. After the questionnaire is returned to WFUSM, the data will be transcribed to data form for analysis.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting any data on this study or others with similar study design.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 13. The total number enrolled study-wide is 245, if multi-site study. This study was closed to enrollment 15 November 2001.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 79804 - Issues of Survivorship Among Breast Cancer Survivors

KEYWORDS:

PRINCIPAL INVESTIGATOR: Joseph J. Drabick COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: C

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 27 February 2001

### STUDY OBJECTIVE

1. To determine the prevalence of physical, economic, psychosocial and spiritual consequences of survivorship, including issues related to reproduction, menopause, osteoporosis, post-mastectomy/lumpectomy pain, and lymphedema among a cohort of disease-free long-term breast cancer survivors.
2. To determine how these problems affect overall health related quality of life (HRQL).

### TECHNICAL APPROACH

Potentially eligible patients were identified by research personnel at Wake Forest University School of Medicine (WFUSM) and by research personnel at WRAMC. An introductory letter was sent to potential patients. About one week after the letters were sent, the patients were contacted by phone by research personnel from WRAMC to further explain the study, answer questions, assess interest in participation in the study, and arrange for a follow-up appointment at WRAMC to complete the consent process. After registration to the study, a professional research interviewer from WFUSM will send a questionnaire to the patient. After the questionnaire is returned to WFUSM, the data will be transcribed to data form for analysis.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting any data on this study or others with similar study design.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 13. The total number enrolled study-wide is 245, if multi-site study. This study was closed to accrual 15 November 2001. CALGB is not requiring any more data collection on any study subjects. This study can now be closed here at WRAMC.

### CONCLUSIONS

Close study.



## DETAIL SUMMARY SHEET

TITLE: CALGB 89904 - A Randomized Phase II Study of Gemcitabine/Cisplatin, Gemcitabine/Docetaxel, Gemcitabine/Irinotecan, or Fixed Dose Rate Infusion Gemcitabine in Patients with Metastatic Pancreatic Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 20 March 2001

### STUDY OBJECTIVE

The primary objective of this study is to assess survival rate of patients with metastatic pancreatic cancer treated with one of four novel gemcitabine-based combination chemotherapy regimens.

Secondary objectives are to estimate the time to disease progression with metastatic pancreatic cancer treated with one of four chemotherapy regimens, to estimate the biomarker CA19-9 response to each regimen, to correlate the CA19-9 response with radiologic response and survival, and to assess the toxicity of each chemotherapy regimen in this patient population.

### TECHNICAL APPROACH

Patients will be randomized to one of the four chemotherapy arms - Gemcitabine alone or in combination with one of the following chemotherapy agents that have been approved by the FDA for other cancers - Cisplatin, Docetaxel, or Irinotecan. Depending on the chemotherapy regimen assigned, the patient will be treated weekly times three weeks with one week of rest, or weekly times two weeks with one week of rest. Patients will be treated until disease progression, if unacceptable toxicities develop, or the patient withdraws consent.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this study or from any study with similar study design.

The number of subjects enrolled to the study since last APR at WRAMC is 2 and the total enrolled to date at WRAMC is 4. The total number enrolled study-wide is 70, if multi-site study. Grade 4 toxicities include 2 neutrophils/granulocytes, 2 leukocytes (total WBC), 2 hemoglobin (Hgb), 2 SGOT (AST), 6 maximum toxicity. Adverse events reported 27 November 2001, 18 December 2001, and 21 January 2003.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 99903 - A Phase II Study of Arsenic Trioxide (NSC #706362, IND #57974) in Urothelial Cancer

KEYWORDS: Phase II; Arsenic Trioxide; Urothelial Cancer; IND (Investigational New Drug)

PRINCIPAL INVESTIGATOR: MAJ Joseph Flynn MC

DEPARTMENT: Medicine

STATUS: C

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 17 April 2001

### STUDY OBJECTIVE

1. To determine the efficacy of arsenic trioxide in patients with measurable urothelial carcinoma of the bladder, urethra, or renal pelvis.
2. To determine the toxicity of arsenic trioxide administered to patients with urothelial cancer.

### TECHNICAL APPROACH

Adult healthcare beneficiaries with a diagnosis of transitional cell carcinoma of the bladder, urethra, ureter or renal pelvis, seen in the Hematology-Oncology Clinic at WRAMC will be evaluated for study eligibility. All females must have a negative pregnancy prior to study entry. Prior to each cycle, female subjects of childbearing potential must have a negative pregnancy test and be using an adequate method of contraception. Arsenic trioxide 0.3mg/kg/day will be infused over one hour daily for five consecutive days every four weeks. (One week of treatment, three weeks rest). Every two cycles, the patients will be restaged for response. Lab work (CBC and chemistries) will be done prior to every cycle. An EKG will be done prior to every cycle. Patients will have a physical exam and toxicity assessment prior to every cycle. Continuation of therapy will be based on severity of toxicities and disease response. After the first twelve patients (group-wide) are enrolled, the study will be suspended to accrual to evaluate the response rate. If one or fewer responses are observed, the trial will be terminated. If two or more patients respond, an additional 23 patients will be enrolled. If six or more responses are observed at the end of the second stage, the study will be considered for a Phase III setting.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are no publications reporting data from this or other studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 13, if multi-site study. There were no Grade 4 toxicities reported. No adverse events reported. This study was closed to accrual effective March 15, 2002, due to insufficient responses in the enrolled patients. WRAMC enrolled 0 patients on this study. This study can be closed here at WRAMC.

Ref: CALGB June 2002 Statistical Report

### CONCLUSIONS

Too early. Administrative comments reports closed due to insufficient responses in the enrolled patients.

## DETAIL SUMMARY SHEET

TITLE: CALGB 49805 - A Phase III Randomized Double Blind Study of Letrozole Versus Placebo in Women with Primary Breast Cancer Completing Five or More Years of Adjuvant Tamoxifen

KEYWORDS: Randomized; Double Blinded; Letrozole; Placebo; Breast Cancer; Tamoxifen

PRINCIPAL INVESTIGATOR: Joseph Drabick, COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 24 July 2001

### STUDY OBJECTIVE

Primary: To determine the disease-free survival and overall survival (all cause mortality) for women who have previously received  $\geq$  five years of adjuvant tamoxifen, randomized to receive either letrozole 2.5 mg daily or placebo daily for five years. Secondary: To evaluate the incidence of contralateral breast cancer. To evaluate the long term clinical and laboratory safety of letrozole with special attention on: lipid profile as assessed by blood sampling (in a limited number of centers); cardiovascular morbidity and mortality (i.e., significant coronary heart disease, which includes myocardial infarctions and angina requiring percutaneous transluminal coronary angioplasty of coronary artery bypass graft, fatal and nonfatal strokes and all vascular deaths) as assessed by reported toxicity; the incidence of all bone fractures (with particular emphasis on hip and wrist fractures as indicators of osteoporosis) as assessed by reported toxicity; changes in bone density (in a limited number of centers); common toxicities as assessed by reported toxicity. To evaluate overall quality of life.

### TECHNICAL APPROACH

Patients having completed five years of Tamoxifen ending <2 months from study entry will be randomized to Letrozole or placebo. This is a double-blinded study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data from this or other studies with similar study design.

The number of subjects enrolled to the study since last APR at WRAMC is 1 and the total enrolled to date at WRAMC is 8. The total number enrolled study-wide is 5179, if multi-site study. No toxicities reported on this study. Adverse events reported July 22, 2002. This study was closed to accrual effective May 31, 2002.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 49801 - Phase III Trial of Tamoxifen Alone vs. Tamoxifen Plus Radiation for Good Risk Ducts Carcinoma In-Situ (DCIS) of the Female Breast

KEYWORDS:

PRINCIPAL INVESTIGATOR: Ketchum, Lloyd CPT MC  
ASSOCIATES:

DEPARTMENTS: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 31 August 2001

### STUDY OBJECTIVE

In the defined good-risk group, assess the role of whole breast radiation plus tamoxifen compared to tamoxifen alone in decreasing or delaying the appearance of local failure, both invasive and *in situ*, and preventing the need for mastectomy. Assess distant disease-free survival to affirm the hypothesis that the proportion of patients in either arm who fail with progression to invasive local disease can be successfully salvaged with further definitive local therapy and adjuvant systemic therapy as appropriate to the individual case.

### TECHNICAL APPROACH

These patients have been diagnosed in the early stage of breast cancer. The anti-estrogen hormone tamoxifen may be appropriate to use after the surgeon has removed the cancer. In this study, treatment with tamoxifen will be compared to treatment with tamoxifen plus radiation therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this and other studies with similar design in literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 204, if multi-site study. There were no reported toxicities of Grade 4 or higher.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 159902 - Molecular Markers of Pleural Involvement In Resected Non-small Cell Lung Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENTS: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 31 August 2001

### STUDY OBJECTIVE

To confirm the relationship between the presence of malignant cells in pleural lavage liquids and disease-free survival. To determine the incidence of expression of K-ras codon 12 mutation, mRNA encoding surfactant protein-A, or telomerase activity, in cells found in pleural lavage of patients undergoing thoracotomy for surgical resection of NSCLC. To examine the relationship between the presences of K-ras mutations, mRNA encoding surfactant protein-A, and telomerase activity in cells obtained by pleural lavage and the time to recurrence of disease, patterns of failure, and survival. To determine whether the presence of cells determined malignant by cytologic analysis in pleural lavage is associated with expression of K-ras mutations, mRNA encoding surfactant protein-A, or telomerase activity. To correlate the identification of K-ras mutations in pleural lavage cells with the presence of K-ras mutations in the primary tumor specimens.

### TECHNICAL APPROACH

Immediately after the chest is entered during thoracotomy it will be examined by the operating surgeon for gross evidence of metastases. If appropriate disease type and stage are found, the surgeons will lavage the pleura with 300ml of normal saline. The lavage liquid will be collected by suction, heparin added, and placed on ice.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this study since last APR.

The number of subjects enrolled to the study since last APR at WRAMC is 1 and the total enrolled to date at WRAMC is 4. The total number enrolled study-wide is 216, if multi-site study. No Grade 4 toxicities reported.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 509901 - Phase II Study of Melanoma Vaccine (NSC#683472/675756, IND 6123) and Low-Dose, Subcutaneous Interleukin-2 in Advanced Melanoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Gorak, Edward J. MAJ MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: C  
INITIAL APPROVAL DATE: 14 September 2001

### STUDY OBJECTIVE

Estimate clinical response rate to gp 100:209-217(210M) melanoma vaccine and low-dose, subcutaneous interleukin-2. Observe induction of gp 100:209-217(210M) reactive T cells in peripheral blood mononuclear cells (PBMC) by ELISPOT assay for interferon gamma. Observe response duration and progression free intervals. Observe CALGB accrual rate for this phase II study in metastatic melanoma. Establish feasibility of HLA subtyping and ELISPOT monitoring.

### TECHNICAL APPROACH

Study treatment will consist of two vaccinations of the investigational drug known as melanoma vaccine, followed by five days of IL-2 given by a subcutaneous injection, and then one week later, another five days of IL-2 given by a subcutaneous injection.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data from studies with similar design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 27, if multi-site study. No grade 4 toxicities reported.

This study is closed to accrual effective 15 July 2003. We will be closing this study here at WRAMC – zero patients enrolled.

Ref: CALGB Statistical Report Jun 03

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: Epstein-Barr Virus as an Etiologic Agent for Hodgkin's Disease - A Nested Case-Control Study

KEYWORDS: Pre-diagnosis serology, EBV, Hodgkin's Disease, immunology, EBER.

PRINCIPAL INVESTIGATOR: Joseph Drabick COL MC

ASSOCIATES: Lynn Levin, Ph.D., M.P.H.

DEPARTMENT: Medicine

STATUS: C

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 5 December 2000

### STUDY OBJECTIVES

The focus of this study is to integrate the pre-diagnosis serology in relation to the molecular status of Hodgkin's Disease (HD) cases in order to elucidate the interplay of host and viral factors in the pathogenesis of this disease. For the serologic analysis, we will conduct a nested case-control study of incident cases and matched controls identified from the Department of Defense Serum Repository (DoDSR). We expect a total of 300 cases and 900 controls. For each case, the diagnostic tissue block will be obtained from medical treatment facilities and medical centers in the Army, Navy and Air Force. Tissue blocks from all cases will be tested for EBV genome status. These data will be evaluated for consistency with three models of HD pathogenesis:

1. The EBV is solely related to EBV-genome positive HD with EBV-genome negative disease due to non-viral causes;
2. HD is a virally induced malignancy with the EBV responsible for EBV-genome positive disease and another unidentified virus(es) linked to EBV-genome negative disease;
3. The EBV plays a crucial role in the pathogenesis of essentially all HD cases but the genome is selectively lost in some patients.

### TECHNICAL APPROACH

To complete the study at WRAMC, tissue blocks were requested for a total of 24 HD cases that were either initially evaluated at WRAMC or referred to WRAMC. The blocks will be returned to the WRAMC Anatomic Pathology Service once slides are prepared at the Armed Forces Institute of Pathology (AFIP).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 9 and the total enrolled to date at WRAMC is 19. The total number enrolled study-wide is 308, if multi-site study.

### CONCLUSIONS

To examine the Epstein-Barr virus (EBV) serologic profile preceding diagnosis in relation to the molecular status of Hodgkin's lymphoma (HL) cases, we conducted a nested case-control study of 112 incident HL cases, and matched controls from active-duty military personnel with archived serum in the US Department of Defense Serum Repository. Tissue blocks from cases were tested for EBV genome status. In conditional logistic regression analyses of 32 EBV-positive HL and matched controls, statistically significant risks were associated with elevated anti-EBV serum antibody titers for EA-D [OR=3.04 (95% CI=1.05-8.80)], EA-R [OR=3.93 (95% CI=1.14-13.53)], EBNA-2b [OR=5.05 (95% CI=1.25-20.42)] and the ratio of EBNA-1 to EBNA-2 <1 [OR=13.41 (95% CI=1.58-113.81)]. When the titers were mutually controlled in multivariate analyses, the only association that approached significance was with EBNA-1/EBNA-2, indicative of defective control of latent EBV infection. Analyses of eighty EBV-negative cases relative to their matched controls revealed a strikingly different pattern as null findings were found with all antibody titers. Moreover, a strong association was noted for EBNA-1/EBNA-2 in EBV-positive HL relative to EBV-negative HL. This contrasting antibody profile suggests differences in host response to the virus as well as differences in the natural history of disease based on EBV genome status.

## DETAIL SUMMARY SHEET

TITLE: Microarray Analysis of Breast Cancer - A Pilot Feasibility Study

KEYWORDS: breast cancer, microarray, gene expression profiles

PRINCIPAL INVESTIGATOR: McGrail, Lisa MAJ MC

ASSOCIATES: Shriver, Craig COL MC

DEPARTMENT: Medicine

STATUS: C

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 9 January 2001

### STUDY OBJECTIVE

Determine the feasibility of developing tissue procurement and processing procedures for future microarray projects. Analyze gene expression profiles between specimens of matched normal to cancerous breast tissue via microarray technology.

### TECHNICAL APPROACH

There have been no modifications to the methodology. In summary, tissue specimens were obtained after definitive surgical resection of a breast tumor. The surgeon and pathologist determined together if there was excess tissue to be used in this study. Fifty percent of the tumor tissue and fifty percent of the normal tissue were immediately prepared and processed for microarray analysis by the PI. The other fifty percent of the tumor was stored and then transported to Windber Research Institute (WRI) for microarray analysis. All tissue was devoid of patient identifiers. All tissue was coded with an identifier.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since the last APR, no additional patients have been enrolled. There have been no adverse events and no patients have withdrawn from the study. No modifications or amendments have been made. The tissue allocated for microarray analysis at Georgetown University has been consumed in the processing and the remaining tissue destroyed as of the last APR. In summary, of the tissue remaining at the Windber Research Institute (WRI), proteins were isolated from eight samples and RNA from fifteen samples. Six of the protein samples were analyzed by 2D-DIGE whereas seven of the RNA samples were analyzed by cDNA array analysis (Table 1). The number of subjects enrolled to the study since last APR at WRAMC is 0. The total enrolled to date at WRAMC is 11.



Work Unit # 01-16002 [Continued]

Table 1

Sample Code	Type	Date Sample Obtained	Tissue in Freezer	Wt (g)	Protein Extracted from Tissue/Used	RNA Extracted from Tissue/Used	DNA extracted from Tissue/Used	Amt. Of Tissue &/or Product Left (%)
P1NW	Biopsy	02/12/01	No	0.63	Yes/No	Yes/Yes	No	50
P1CW	Biopsy	02/12/01	No	0.62	Yes/No	Yes/No	No	50
P2NW-1	Biopsy	02/23/01	No	3.7	Yes/No	Yes/No	No	95
P2NW-2	Biopsy	02/23/01	No	1.51	Yes/No	Yes/No	No	95
P2NW-Node	Biopsy	02/23/01	Yes	0.97	No	No	No	0
P3NW	Biopsy	03/08/01	No	0.73	No	Yes/No	No	95
P3CW	Biopsy	03/26/01	No	0.52	No	Yes/No	No	95
P4NW	Biopsy	03/26/01	No	----	Yes/No	Yes/No	No	95
P4CW	Biopsy	03/26/01	No	0.25	Yes/No	Yes/No	No	95
P5NW	Biopsy	03/26/01	No	0.16	No	Yes/Yes	No	5
P5CW	Biopsy	04/17/01	Yes	0.17	No	Yes/Yes	No	5
P6NW-1	Biopsy	04/17/01	Yes	2.45	No	No	No	100
P6NW-2	Biopsy	04/17/01	Yes	2.19	No	No	No	100
P7N-L	Biopsy	04/20/01	Yes	15.66	No	No	No	100
P7N-R	Biopsy	05/01/01	No	27.84	No	Yes/No	No	100
P8NW	Biopsy	05/01/01	No	1.06	Yes/Yes	Yes/Yes	No	0
P8CW	Biopsy	05/22/01	No	0.8	Yes/Yes	Yes/Yes	No	0
P9NW	Biopsy	05/22/01	No	0.35	No	Yes/Yes	No	50
P9CW				0.39	No	Yes/Yes	No	50

### CONCLUSIONS

This pilot study laid the groundwork for the much larger CBCP tissue banking initiative. We clearly established that tissue procurement for microarray analysis is highly feasible, and the procedures and processes used here have been instrumental in establishing the methods used in the CBCP tissue protocols. Given that those protocols are actively accruing, we plan to focus our efforts on analyzing paired tissue and clinical data, and close this pilot study. There is no further analysis of tissue planned or on-going, and all remaining tissue will be destroyed.

## DETAIL SUMMARY SHEET

TITLE: Expression of Human Papilloma Virus in Second Primary Malignancies Associated with Chronic Lymphocytic Leukemia

KEYWORDS:

PRINCIPAL INVESTIGATOR: Flynn, Joseph M. CPT MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: C  
INITIAL APPROVAL DATE: 13 March 2001

### STUDY OBJECTIVE

The objectives of this protocol are to ascertain whether human papilloma virus may be identified in conjunction with second primary tumors associated with patients with Chronic Lymphocytic Leukemia.

### TECHNICAL APPROACH

Tumors identified in patients with CLL and matched controls are being analyzed by PCR for determination of presence of human papilloma virus. We seek the ability to increase the number of cases studied as more of the original 43 patients from #1606 have been retrieved. This will add to the power of this study. The initial number requested was based on a request by the DCI for a number of tissue blocks that we were able to retrieve at that time.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The study to date has accrued 20 tumors from the control group and 20 from the CLL group. No further accrual has been recorded. An interim analysis was performed and there was demonstrated statistical significance with appropriate power. An addendum was submitted in response to these results.

The number of subjects enrolled to the study since last APR at WRAMC is 40 and the total enrolled to date at WRAMC is 40.

### CONCLUSIONS

There is a statistically significant difference between the expression of human papilloma virus in those with tumors related to CLL and those who do not have CLL. HPV was found in 8 of 15 tumors in patients with CLL and 0 of 16 tumors in the control population. Further, length of disease seemed to impact on the association.

## DETAIL SUMMARY SHEET

**TITLE:** A Multicenter, Phase III Randomized Trial for Stage IIIB or IV NSCLC Comparing Weekly Taxol (Paclitaxel) and Carboplatin (Paraplatin) Regimen Versus Standard Taxol and Carboplatin Administered Every Three Weeks, Followed by Weekly Taxol

**KEYWORDS:** Phase III; NSCLC; weekly versus every three weeks; Taxol; Carboplatin

**PRINCIPAL INVESTIGATOR:** MAJ Carl Willis, MC

**ASSOCIATES:** LTC Rickey Myhand, COL Joseph Drabick, COL Alfred Brooks, MAJ Joseph Flynn

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Hematology-Oncology

**INITIAL APPROVAL DATE:** 26 June 2001

### STUDY OBJECTIVE:

To determine the overall patient survival rate for each of the two treatment regimens outlined in this study, and to see if the experimental regimen is as effective as or better than the standard treatment. The secondary objectives are to determine the time to disease progression for each regimen, to determine the objective response rate of the two treatment regimens, and to evaluate the safety and toxicity of the treatment.

### TECHNICAL APPROACH

Patients will be randomized to receive either Taxol 100 mg/ml weekly for 3 weeks, 4<sup>th</sup> week rest with Carboplatin AUC 6 given after Taxol on Day 1 only of each cycle (1 cycle = 4 weeks) for a total of 4 cycles (16 weeks) or Taxol 225 mg/ml followed by Carboplatin AUC 6 once every 3 weeks, repeat for 4 cycles (for a total of 12 weeks). Both regimens will be followed by weekly Taxol at 70mg/m<sup>2</sup> and will be continued until development of progressive disease, development of intercurrent illness, development of intolerable toxicity, patient refusal of further treatment, investigator decision to terminate treatment, or delay in treatment > 2 weeks (excluding week(s) of rest in treatment cycle).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A total of six patients were enrolled in this study at WRAMC. The study has met accrual and is closed to further accrual. DCI/HUC has been notified of the study's closure. Four of the WRAMC patients have died of their metastatic NSCLC. They were off study therapy at the time of their deaths. The other two patients have been removed from this study because of progressive disease during protocol therapy. Reports of six adverse events have been reported by our service to the WRAMC HUC.

The number of subjects enrolled to the study since last APR at WRAMC is 4 and the total enrolled to date at WRAMC is 6. The total number enrolled study-wide is 444, if multi-site study.

### CONCLUSIONS

No conclusions have been reported. Statistical analysis of the data continues.

## DETAIL SUMMARY SHEET

**TITLE:** An Open-Label, Multicenter, Randomized, Phase III Study Comparing Oral Topotecan/Cisplatin Versus Etoposide/Cisplatin as Treatment for Chemotherapy-naïve Patients with Extensive Disease-Small Cell Lung Cancer.

**PRINCIPAL INVESTIGATOR:** MAJ Carl Willis, MC

**ASSOCIATES:** CPT Joseph Flynn MC

**DEPARTMENT:** Medicine

**SERVICE:** Hematology-Oncology

**STATUS:** C

**INITIAL APPROVAL DATE:** 31 July 2001

### STUDY OBJECTIVE

The primary objective is to compare overall survival using Kaplan-Meier estimates in chemotherapy-naïve patients with extensive stage small cell lung cancer (SCLC) randomized to treatment with oral topotecan plus cisplatin or cisplatin plus etoposide. This trial will test the hypothesis that the regimen will prolong patient survival compared to the standard regimen. The secondary objective is to compare the response rates, response duration, time to progression, tolerability, and patient-perceived disease status and well being for patients in each treatment arm.

### TECHNICAL APPROACH

This is an open-label, multicenter, randomized phase III study. Patients will be stratified according to gender, performance status (0, 1, or 2), LDH (normal or elevated), and country. Eligible patients will be randomized to one of two treatment arms: Topotecan (1.7 mg/m<sup>2</sup>/day) administered orally on days 1-5 with Cisplatin (60 mg/m<sup>2</sup>/day) administered intravenously on day 5 every 21 days; OR, Cisplatin (80 mg/m<sup>2</sup>/day) on day 1 with Etoposide (100 mg/m<sup>2</sup>/day) administered intravenously on days 1-3 every 21 days (21 days = 1 course/cycle). Treatment duration will depend on the response to treatment. A maximum of 6 courses should be administered. All patients should receive at least 4 courses of treatment unless one or more of the following occur: disease progression, development of intercurrent illness, development of intolerable toxicity, patient refusal of further treatment, investigator decision to terminate treatment, or delay in treatment > 2 weeks beyond day 21.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This protocol was amended in November 2001 to allow patients to be treated for greater than 6 cycles, or 2 cycles beyond best response. It was again amended in September 2002 to increase the overall sample size to 830 patients from 760 patients. At WRAMC, 1 patient was enrolled on study. He experienced 1 SAE, (syncopal episodes) resulting in hospitalization for evaluation. These syncopal episodes were attributed to a pneumonia that he was found to have. He went on to receive 6 cycles of therapy, achieving a partial response as his best response.

Over the course of this study 39 safety reports/AEs were from GlaxoSmithKline and reported to the WRAMC IRB. These AEs occurred in patients being treated on this protocol at other sites, or on other protocols with the study medication.

The number of subjects enrolled to the study since last APR at WRAMC is 1 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 859, if multi-site study.

### CONCLUSIONS

This study met target enrollment and was closed to accrual effective 10 December 2002. Analysis of data is ongoing by GlaxoSmithKline.

## DETAIL SUMMARY SHEET

TITLE: Reference Values for Impulse Oscillometry in Normal Adults

KEYWORDS: spirometry; impulse oscillometry; normal reference values

PRINCIPAL INVESTIGATOR: Hnatiuk, Oleh LTC MC  
ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Pulmonary & Critical Care Medicine

INITIAL APPROVAL DATE: 21 November 2000

### STUDY OBJECTIVE

To establish reference values for impulse oscillometry in a population of normal adults.

### TECHNICAL APPROACH

Two phase prospective cohort trial. First phase to be performed at WRAMC PFT Lab and involves testing 50 asymptomatic individuals > 18 years old within the hospital staff and population with spirometry and, if normal, with an impulse oscillometer. The second phase (submitted as a separate protocol) involves identifying military posts with large active duty populations and, following local approval, testing each subject with spirometry and impulse oscillometry.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are no new studies evaluating normative data for impulse oscillometry. The manufacturer and also pulmonologists across the country are now very interested in identifying the proper mouthpiece to use and developing a normative data set in the US that will include individuals of different races. An addendum approved in June 2002 allowed us to change from two impulse oscillometry machines to one. However, due to continued software problems (both procurement and on-site glitches), we have only recently begun data acquisition. The company that donated the original oscillometry equipment has undergone a merger with a larger firm. Working with this new conglomerate has proven to be very difficult in terms of obtaining updated software and technical support for free, since they are very motivated by profit.

The number of subjects enrolled to the study since last APR at WRAMC is 1 and the total enrolled to date at WRAMC is 1.

### CONCLUSIONS

Despite our difficulties, we have persevered, and have begun data collection. PI does not anticipate obtaining data sets for fifty individuals to take another full year.

## DETAIL SUMMARY SHEET

TITLE: Quality Management in Sleep Medicine via Telemedicine - Overseas Online Transfer of Polysomnograms via Internet File Transfer Protocol from Landstuhl Army Medical Center to Walter Reed Army Medical Center

KEYWORDS: Telemedicine, sleep medicine, quality control

PRINCIPAL INVESTIGATOR: Kristo, David LTC MC

ASSOCIATES: Eliasson, Arn COL MC; Thomas Bigott

DEPARTMENT: Medicine

STATUS: O

SERVICE: Pulmonary & Critical Care Medicine

INITIAL APPROVAL DATE: 15 May 2001

### STUDY OBJECTIVE

To compare the results of scoring and interpretation of sleep study data at the site in Landstuhl Regional Medical Center versus the scoring and interpretation results of the same online sleep study data transferred at WRAMC by a sleep specialist for quality control purposes.

### TECHNICAL APPROACH

Subjects receiving sleep studies at Landstuhl Regional Medical Center (LRMC) will have raw (unscored, uninterrupted) sleep study data sent to Walter Reed Army Medical Center (WRAMC). Transmission of sleep studies will be done via Internet, or, in case of Internet difficulties, sent on optical disk via registered mail. (Modification allowing studies to be sent via registered mail was proposed in Addendum 1 and approved.) Also, subjects will fill out three standard sleep questionnaires on the night of the study – the Berlin Questionnaire, Epworth Sleepiness Scale, and WRAMC Sleep Questionnaire – and results will be faxed to WRAMC physicians. An uninvolved administrator will scrub all patient data of identifying information prior to sending to WRAMC and scoring and interpretation at WRAMC.

Physicians at both LRMC and WRAMC will independently examine each subject's sleep study. Then they will compare the interpretations for each study. The project will evaluate the technology and effective use of telemedical principles. The content of the transferred information will in no way be used to affect clinical care decisions until the study is concluded.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at LRMC is 32 and the total enrolled to date at LRMC is 56. All sleep studies have been sent to WRAMC on optical disk via registered mail because of extreme difficulties encountered in the attempt to transmit sleep study data electronically. To date, forty-one studies have been scored, and physicians at WRAMC have interpreted none. Five studies on one optical disk were unreadable, and cannot be included in the study.

During the past year, the sleep lab at LRMC has relocated within the hospital, and their workload has recently changed and intensified due to the war in Iraq. Only half of the proposed 100 participants have been enrolled. It is expected that further progress on this proposal will be slow until resources at LRMC can again focus on routine evaluation of sleep disorders.

No patients have withdrawn from the study, and no patients have had adverse events. No recent literature regarding telemedicine and sleep is relevant to this study.

### CONCLUSIONS

No conclusions have been drawn from this study.

## DETAIL SUMMARY SHEET

**TITLE:** A Comparison Between an Internet Communications Platform and Traditional Medical Care as a Health Care Management Model in Patients with Obstructive Sleep Apnea

**KEYWORDS:** telemedicine, C-PAP, obstructive sleep apnea, compliance, self-efficacy

**PRINCIPAL INVESTIGATOR:** Taylor, Yvonne, DrPH(c), DAC

**ASSOCIATES:** COL Arn Eliasson, MC; LTC David A. Kristo, MC; Tim Andrada; Paula Ephraim, LTC (Ret.)

**DEPARTMENT:** Medicine

**STATUS:** C

**SERVICE:** Pulmonary & Critical Care Medicine

**INITIAL APPROVAL DATE:** 19 June 2001

### STUDY OBJECTIVE

To compare compliance with Continuous Positive Airway Pressure regimens to treat Obstructive Sleep Apnea (OSA) between OSA patients receiving standard outpatient management and those receiving standard care augmented by a "Health Buddy" Internet health care provider interface.

### TECHNICAL APPROACH

The study design was a randomized controlled trial. Two groups were enrolled to consist of an intervention and a control group. The intervention group received the telemedicine management model of care and the control group received the traditional standard of care management model (usual care). Dependent variables consisted of CPAP use, functional status, client satisfaction and general self-efficacy. Outcome variables were measured at baseline and thirty days later.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study findings revealed that the telemedicine management model of care made no significant difference in CPAP use, functional status, client satisfaction and general perceived self-efficacy compared to usual care. This study has been completed and to date 114 patients completed the study. Nine patients in the telemedicine group were withdrawn from the study due to failure to activate the telemedicine technology or use CPAP for at least 30 days. One patient was withdrawn from the traditional care group due to failure to use CPAP for at least 30 days.

The number of subjects enrolled to the study since last APR at WRAMC is 113 and the total enrolled to date at WRAMC is 133.

### CONCLUSIONS

The results of this study offer evidence that the application of a telemedicine management model of care made no statistically significant difference in increasing the duration and frequency of nasal CPAP hours of use compared to a traditional management model of care. Statistically and clinically significant changes also were not detected in functional status, client satisfaction and general self-efficacy. The results suggest that daily activation of the Health Buddy computer during the 30-day observation period did not influence CPAP use and subsequently did not make a difference in functional status, general perceived self-efficacy and client satisfaction.

## DETAIL SUMMARY SHEET

TITLE: Comparison of F-18 FDG Coincidence PET with Tc-99m Depreotide in the Evaluation of Pulmonary Lesions

KEYWORDS:

PRINCIPAL INVESTIGATOR: Wink, Jennifer, CPT MC  
ASSOCIATES:

DEPARTMENT: Medicine

STATUS: C

SERVICE: Pulmonary & Critical Care Medicine

INITIAL APPROVAL DATE: 26 June 2001

### STUDY OBJECTIVE

To compare the accuracy of F-18 Fluorodeoxyglucose (FDG) Coincidence PET with Tc-99m depreotide in the evaluation of pulmonary nodule(s). Correlation will be made with biopsy pathology or radiographic stability. Accuracy of the scans will also be compared with that of physicians' estimate of malignancy and to Bayesian analysis.

### TECHNICAL APPROACH

WRAMC pulmonary physicians using history and physical examination will evaluate subjects and all available chest radiographs and CT scans. A management plan will be determined as indicated to include serial radiographic follow-up, bronchoscopic or percutaneous biopsy, surgical staging or resection. This is standard of care. Nuclear Medicine scans using F-18 FDG or Tc-99m studies will be obtained and reviewed by board-certified nuclear medicine physicians blinded to the pulmonologist's clinical impression and any pathology data. Physician estimate of PCA, Bayesian analysis estimates (for the solitary pulmonary nodules), 18-FDG coincidence results and Tc-99m depreotide results will be compared to actual pathology and to each other. Actual pathology will be defined as histology of biopsy or surgical specimen. Lesions will be defined as benign if they are radiographically stable for two years.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study stopped enrolling patients in December 2002 due to a change in the most up to date technology in the nuclear medicine department. They obtained new equipment that made the use of coincidence imaging obsolete. In addition, Tc-99m was then unavailable in this country for several months.

The previous primary investigator, William Kelly, completed an analysis of the initial 20 patients. This was presented in poster format at the 2002 American College of Chest Physicians. The conclusions are as follows: "Tc-99m depreotide appears to be more accurate than F-18 FDG Coincidence PET in the identification of malignant pulmonary nodules to date." A second poster concluded "Nuclear medicine scanning changed physician suspicion of malignancy enough to change the management of pulmonary nodules in 4 of 20 (20%) of patients enrolled to date. In one case this led to resection of a lung cancer. In the others, unnecessary surgery has been avoided."

The additional 17 patients have not been subsequently included in the analysis because the data did not significantly alter that which had already been reported and 6/17 persons did not complete the required exams.

The number of subjects enrolled to the study since last APR at WRAMC is 15 and the total enrolled to date at WRAMC is 37.

### CONCLUSIONS

Not included in report.



## DETAIL SUMMARY SHEET

TITLE: Delivery of High Concentrations of Inspired Oxygen Using Humidified Oxygen by Nasal Cannula (Vapotherm)

PRINCIPAL INVESTIGATOR: MAJ Melanie L. Guerrero, MC

DEPARTMENT: Medicine

STATUS: O (Abeyance)

SERVICE: Pulmonary & Critical Care Medicine

INITIAL APPROVAL DATE: 31 July 2001

### STUDY OBJECTIVE

To compare the arterial partial pressure of oxygen obtained using Vapotherm, a high-flow, humidified oxygen delivery system via nasal cannula with that using a non-rebreather mask in subjects who require chronic supplemental oxygen.

### TECHNICAL APPROACH

Most inclusion and exclusion criteria can be determined from patient records before the initial telephone call. Thus, telephone calls will be directed only to patients who are believed to meet the criteria. However, confirmation will be sought during the telephone conversation as patient records may be incomplete. Both nasal cannula and non-rebreather mask will be compared in patients with compromised lung function requiring chronic supplemental oxygen. Half of the subjects will use the nasal cannula first; the other half will use a non-rebreather mask first. There will be a washout period of sixty minutes in between, during which patients will receive their normal low-flow oxygen supplementation by nasal cannula. The order will be randomized based on random number generation from a computer program.

On the morning of testing, the protocol will be fully reviewed with the subject. Informed, written consent will be obtained. Outpatient records will be reviewed for evidence of cardiac disease. Patients' charts will also be reviewed to determine the etiology of underlying pulmonary disease. Patients will not be required to synchronize respirations with a metronome as originally planned in the study, as this is deemed unnecessary for data analysis. This is only an additional task for the patient that may be uncomfortable and unnatural in the usual breathing pattern. A PCO<sub>2</sub> of  $\geq 45$  on the first arterial blood gas taken for study purposes would be an exclusion for further participation on the study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

None. PI deployed.

### CONCLUSIONS

None. PI deployed.

## DETAIL SUMMARY SHEET

**TITLE:** A Randomized, Open-Label, Phase III, International Study of Subcutaneous Recombinant IL-2 (Proleukin) in Patients with HIV-1 Infections and CD4+ Cell Counts >300/mm<sup>3</sup> - Evaluation of Subcutaneous Proleukin in a Randomized International Trial (ESPRIT)

**KEYWORDS:** HIV, IL-2, ESPRIT

**PRINCIPAL INVESTIGATOR:** Wortmann, Glenn LTC MC

**ASSOCIATES:** Naomi Aronson, COL MC; Richard Trotta, LTC MC

**DEPARTMENT:** Medicine

**SERVICE:** Infectious Disease

**STATUS:** O

**INITIAL APPROVAL DATE:** 17 October 2000

**New Anniversary Date:** 30 March

### STUDY OBJECTIVE

To compare the effects of subcutaneous recombinant interleukin-2 (SC rIL-2) and no SC rIL-2 on disease progression and death over a 5 year follow-up period in patients with HIV-1 infection and absolute CD4 cell counts of  $\geq 300/\text{mm}^3$  who are taking combination antiretroviral therapy.

### TECHNICAL APPROACH

This is an international, phase III, open-label, randomized trial with a total sample size of 4,000 patients. 2,000 patients will be randomized to SC rIL-2 therapy and 2,000 patients will be randomized to no SC rIL-2 over a two-year period.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Five patients have thus far been enrolled in the study at WRAMC. Two patients have successfully completed three cycles of IL-2 with substantial improvement in their CD4 count. One patient was randomized to the standard-of-care arm and is being followed. One patient enrolled in the study and then decided not to participate. One patient enrolled in the study and was then found ineligible secondary to a history of inflammatory bowel disease (the patient had denied a history of bowel disease during the initial interview). This last patient was never randomized, and thus the total number of patients enrolled at WRAMC on the ESPRIT Annual Report datasheet is four. The ESPRIT datasheet also lists one patient as "lost to follow-up". This accounts for the one patient who voluntarily withdrew from the study (the ESPRIT Annual Report datasheet does not list voluntary withdrawals, and lists all patients not currently in the study as "lost to follow-up").

There has been one SAE at WRAMC. This was a patient who reported having a motor vehicle accident in January that required hospitalization. The SAE was submitted to the IRB the day after we learned of the event. There have been several SAEs at other sites, and those have all been forwarded to the IRB as we received them. We have amended the consent form on several occasions as required by the IRB.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 5. The total number enrolled is 3,686 for this multi-site study.

### CONCLUSIONS

The ESPRIT study remains open to enrollment, and WRAMC will continue to recruit patients for the study.

## DETAIL SUMMARY SHEET

TITLE: Sodium Stibogluconate Treatment of Leishmaniasis

KEYWORDS: Leishmania, pentavalent antimonials, treatment

PRINCIPAL INVESTIGATOR: Aronson, Naomi E. COL MC

ASSOCIATES: Wortmann, Glenn LTC MC, Oster, Charles COL MC, Weina, Peter LTC MC, Goldberg, David COL MC, Benson, Paul COL MC, McEvoy, Peter COL MC, Robinson, Gail RN, Smalls, Cyrilla RN

DEPARTMENT: Medicine

STATUS: O

SERVICE: Infectious Disease

INITIAL APPROVAL DATE: 27 March 2001

### STUDY OBJECTIVE

Provide sodium stibogluconate (IND 14150) for treatment of cutaneous leishmaniasis and mucosal leishmaniasis (pentavalent antimonials currently considered the drug of choice for these infections). Provide sodium stibogluconate as a second line treatment for viscerotropic and visceral leishmaniasis (liposomal amphotericin B is the drug of choice for these types as it is FDA approved for visceral leishmaniasis).

### TECHNICAL APPROACH

Sodium stibogluconate 20 mg/kg/day will be given IV or IM for 20 days for DOD health care beneficiaries meeting inclusion and exclusion criteria. Criteria include a parasitologic or clinicoepidemiologic diagnosis of leishmaniasis and a willingness to have therapy at Walter Reed Army Medical Center.

### PRIOR AND CURRENT PROGRESS

Since last APR, New Eng J Med published randomized clinical trial of treatment of a large number of L major cutaneous cases with fluconazole that showed some acceleration of clinical cure over placebo (8 versus 11 weeks). We published our experience (Clinical Infectious Diseases) with 10 versus 20 days of Pentostam in cutaneous leishmaniasis where statistical significance was not reached but equivalency was suggested. In the absence of initial speciation and worldwide exposure of American military, it remains unclear what role fluconazole and short course Pentostam should play in the management of cutaneous leishmaniasis in our program. There have been two serious adverse events in the trial – one a cautionary overnight admission prior to therapy for cardiac monitoring due to baseline bifascicular block. The other SAE was for acute renal failure requiring admission but reversible, occurring 8 October (after Pentostam treatment in early August 2002) immediately after an AFPT test and associated with max CPK levels of about 1100. Subject was recently back at WRAMC and had a nephrology consult and a week of exercise challenge with no evidence of increased creatinine, although myoglobin and CK were greatly increased with maximal exercise (3/4 PT test on last day). Two subjects have chosen to withdraw from treatment prior to conclusion of 20-day course. Both had primarily personal/social reasons, and one investigator has been a verbal champion of his own work where ten days in a small cohort seemed as good as twenty days, which may have influenced this behavior. All three subjects have reached a clinical cure. All remain active in follow-up.

The number of subjects enrolled to the study since last APR at WRAMC is 3 and the total enrolled to date at WRAMC is 3.

### CONCLUSIONS

Pentostam continues to provide a good clinical cure for cutaneous leishmaniasis albeit with frequent, reversible, yet often uncomfortable adverse events.

## DETAIL SUMMARY SHEET

TITLE: Phase 2b Evaluation of Tetravalent Live-Attenuated Dengue Vaccines

KEYWORDS: Dengue, Challenge, Tetravalent live-attenuated vaccine, Protective immunity

PRINCIPAL INVESTIGATOR: Sun, Wellington COL MC

ASSOCIATES: Robert Gibbons, M.D., MAJ(P), MC (WRAIR), Stephen Thomas, M.D., CPT, MC (WRAMC), David W. Vaughn, M.D., COL, MC (WRAIR), John Statler, M.D., MAJ, MC (WRAMC), Clifton A. Hawkes, M.D., LTC, MC (WRAMC)

DEPARTMENT: Medicine

STATUS: C

SERVICES: Infectious Disease

INITIAL APPROVAL DATE: 31 July 2001

### STUDY OBJECTIVE

#### *Primary Objectives*

To evaluate the safety of giving Dengue-1 (DEN-1) and Dengue-3 (DEN-3) challenge viruses or monovalent vaccine to volunteers previously given tetravalent dengue vaccine.

To determine if tetravalent vaccine recipients who developed neutralizing antibody are protected from clinical disease from homologous serotype challenge virus.

To determine if monovalent revaccination elicits clinical illness and anamnestic antibody response in tetravalent vaccine recipients who did not develop homologous neutralizing antibody.

To evaluate in 2 additional flavivirus naïve volunteers if Dengue-4 (DEN-4) H-241 virus is suitable as a challenge virus that consistently causes dengue fever.

#### *Secondary Objectives*

To characterize cellular immune responses to DEN-1 and DEN-3 challenge viruses in volunteers previously vaccinated with tetravalent vaccine and volunteers without previous flavivirus exposure in order to generate hypotheses on correlates of protection.

To characterize cellular immune responses to monovalent dengue revaccination in volunteers previously vaccinated with tetravalent vaccine.

### TECHNICAL APPROACH

#### *Study Subjects*

Young (age 18-45), consenting, healthy adult volunteers who are either previous participants in live-attenuated tetravalent dengue vaccine trial (experimental groups) or have no previous exposure to flaviviruses (control group) were recruited by advertisement, mail, e-mail or telephone.

#### *Study Design*

This is a descriptive, controlled, open-label Phase 2b study. However, the assignment of the serotype of virus is masked to both the investigators and volunteers.

The Challenge arm of the study consists of 10 volunteers from previous tetravalent dengue vaccine studies conducted at the Walter Reed Army Institute of Research (WRAIR) and the Center for Vaccine Development (CVD) at the University of Maryland at College Park. Neutralizing antibody status to all 4 serotypes following vaccination in these volunteers is known. Up to 5 volunteers with serotype-specific antibody to DEN-1 or DEN-3 will be given DEN-1 or DEN-3 challenge virus respectively.

The Revaccination arm of the study consists of up to 12 additional volunteers from the same CVD studies. For each of the 6 vaccine viruses used in previous tetravalent vaccine studies (2 DEN-1, 2 DEN-4, 1 DEN-2 and 1 DEN-3) two vaccinated volunteers with no antibody to that virus will be given the respective monovalent vaccine

#### Work Unit # 01-19003 [*Continued*]

virus. Only 2 volunteers were recruited for this arm of the study, thus only the DEN-3 monovalent vaccine was used for this arm.

The Control arm of the study consists of up to 6 flavivirus-naïve volunteers. Up to two will receive either DEN-1, DEN-3 or DEN-4 challenge virus.

#### *Dose, Schedule and Route*

All volunteers will receive a single 0.5 ml undiluted dose of challenge or vaccine virus subcutaneously in the deltoid region.

#### *Study Endpoints*

1. Presence or absence of clinical disease from challenge virus in antibody-positive vaccinated individuals.
2. Decreased viremia from challenge virus in antibody-positive vaccinated individuals.
3. Clinical safety of monovalent revaccination in antibody-negative vaccinated individuals.
4. Neutralizing antibody response after revaccination in previously antibody-negative vaccinated individuals.
5. Development of dengue fever in the control volunteers given challenge virus.

#### *Statistics and Analysis*

Data analysis will be primarily descriptive in this exploratory study given the small number of volunteers in each test article group. The occurrence of clinical symptoms, antibody responses, and viremia will be recorded and tabulated for each volunteer and compared between the 3 arms of the study and between the 2 serotypes of challenge viruses.

#### *Modifications*

One modification was to allow the use of baseline chest X-rays and abdominal ultrasounds performed in December 2001. Original protocol had required all baseline labs to be done within 60 days of inoculation. This modification was necessary due to a delay of the starting date of the study from 2 January 2002 to 24 May 2002. The reason for the delay of the protocol was to allow the completion of safety testing on the DEN-1 challenge virus. There are no other modifications pertinent to WRAMC part of the protocol.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There is no new literature on dengue challenge study in human volunteers. The number of subjects enrolled to the study was 18; 6 were admitted to WRAMC during the course of the study.

Study was conducted with masking of the challenge or DEN-3 vaccine virus serotype in the 12 volunteers in the Challenge and Revaccination Group. Virus assignment was unmasked to the Principal Investigator on 1 July (Study Day 37).

#### *Modifications*

The only modification was to allow the use of baseline chest X-rays and abdominal ultrasounds performed in December 2001. Original protocol had required all baseline labs to be done within 60 days of inoculation. This modification was necessary due to a delay of the starting date of the study from 2 January 2002 to 24 May 2002. The reason for the delay of the protocol was to allow the completion of safety testing on the DEN-1 challenge virus.

#### *Adverse Events*

There were no serious adverse events. Six volunteers, 3 (WR877-02, WR877-09 and WR877-12) in the Challenge Group and 3 (WR877-13, WR877-15 and WR877-17) in the Control Group were hospitalized at WRAMC when they developed fever, as per protocol. WR877-12's diagnosis turned out to be a tooth abscess while the remaining 5 were considered to be dengue fever. All volunteers recovered clinically without sequelae.

Two Control volunteers, WR877-15, who received DEN-4 and WR877-13, who received DEN-3, developed elevations of AST/ALT. WR877-15 developed AST of 73 IU/ml (normal 21-72) on Day 17 only. WR877-13

Work Unit # 01-19003 [Continued]

developed elevated AST during Day 9 to Day 17, which peaked at 367 IU/ml on Day 13. ALT was elevated on Day 11 to Day 24 that peaked at 291 IU/ml on Day 13. All elevations returned to normal. Volunteer WR877-13 was also the only volunteer in the study to develop thrombocytopenia at 94,000 and 92,000/ml on Day 10 and 11 respectively. Of the previous tetravalent vaccinees in the Challenge arm, only volunteers who received DEN-3 challenge virus developed any AST/ALT abnormalities. Of these three, two had clinical dengue and the other was asymptomatic. WR877-02 had elevated AST (peak 597 IU/ml on Day 9) from Days 6 to 16 and elevated ALT (peak 977 IU/ml on Day 9) from Days 6 to Day 24. WR877-03 had elevated AST Days 5 to 17 and elevated ALT (peak 428 IU/ml on Day 9) from Days 6 to Day 24. Volunteer WR877-05, who was asymptomatic, developed minor AST elevation of 48 IU/ml on Day 9 only. Her ALT was elevated on Day 9 to Day 11 with peak of 85 (normal 9-52 IU/ml). All abnormalities in AST/ALTs resolved by Study Day 30. No volunteers in the Challenge or Revaccination Group developed thrombocytopenia, a sine qua non of dengue hemorrhagic fever. No volunteers developed a positive tourniquet test, another indicator of capillary leakage.

The dengue virus human challenge study, which forms the basis of this study, was completed. Five subjects previously vaccinated with the WRAIR tetravalent dengue vaccine were challenged with DEN-1 low-passage virus and another five volunteers were challenged with DEN-3. There were 2 flavi-virus naïve control volunteers who each received DEN-1 or DEN-3. The results are summarized below:

Den-1 Challenge (Dose =  $10^3$  pfus given subcutaneously)

Volunteer#	Months since last vaccination	Pre-challenge Neutralizing Antibody titer <sup>-1</sup>				Days of viremia*	Peak viremia titer*	Clinical dengue disease
		Den-1	Den-2	Den-3	Den-4			
1	39	415	<10	<10	<10	0	0	No
4	12	235	174	20	<10	0	0	No
6	39	<10	<10	<10	<10	0	0	No
7	42	451	94	30	<10	0	0	No
12	42	198	19	42	<10	0	0	No
17(control)	-	<10	<10	<10	<10	1	94	Yes
18(control)	-	<10	<10	<10	<10	3	5760	Yes

\* by TaqMan PCR, titer expressed in genomic copies per ml

Den-3 Challenge (Dose =  $10^5$  pfus given subcutaneously)

Volunteer#	Months since last vaccination	Pre-challenge Neutralizing Antibody titer <sup>-1</sup>				Days of viremia*	Peak viremia titer*	Clinical dengue disease
		Den-1	Den-2	Den-3	Den-4			
2	12	914	233	<10	<10	2	140	Yes
3	39	144	51	<10	<10	3	3150	Yes
5	36	649	57	57	39	1	104	No
9	13	<10	52	16	18	3	1150	Yes
10	12	171	355	116	60	0	0	No
13(control)	-	<10	<10	<10	<10	5	44000	Yes
14(control)	-	<10	<10	20	<10	3	475	Yes

\* by TaqMan PCR, titer expressed in genomic copies per ml

Work Unit # 01-19003 [*Continued*]

Den-3 Revaccination (Dose =  $10^7$  pfus given subcutaneously)

Volunteer#	Months since last vaccination	Pre-vaccination Neutralizing Antibody titer <sup>1</sup>				Days of viremia*	Peak viremia titer*	Clinical dengue disease
		Den-1	Den-2	Den-3	Den-4			
8	41	<10	<10	<10	<10	0	0	No
11	12	336	<10	59	<10	0	0	No

\*by TaqMan PCR, titer expressed in genomic copies per ml

Volunteer 8 developed neutralizing antibody titer of 1:61 one month after revaccination. Volunteer 11 was found to have antibody titer of 1:59 at the time of revaccination and titer was 1:13 after revaccination.

### CONCLUSIONS

1. All 5 volunteers previously vaccinated with tetravalent live-attenuated dengue vaccine were protected against Den-1 virus challenge. One volunteer did not have measurable Den-1 neutralizing antibody at the time of challenge.
2. Two of 5 volunteers previously vaccinated with tetravalent live-attenuated dengue vaccine were protected against Den-3 virus challenge. Three developed dengue fever. The two volunteers protected against challenge had the highest neutralizing antibody prior to challenge.
3. Revaccination with Den-3 resulted in seroconversion in one volunteer who had no previous response to vaccination with the tetravalent vaccine.

Future challenge studies will evaluate dose response of DEN-3 challenge using a dose of  $10^3$  pfus.

## DETAIL SUMMARY SHEET

TITLE: Creation of a Database of Patients at a High Risk for Breast Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Shriver, Craig LTC(P) MC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: O

SERVICE: General Surgery/CBCP

INITIAL APPROVAL DATE: 30 November 2000

### STUDY OBJECTIVE

1. To collect data on all patients 18 and older who present to the Comprehensive Breast Center at WRAMC and are found to be at a high risk for developing breast cancer.
2. To utilize this database to analyze the diagnosis, treatment and treatment outcomes for patients found to be at a high risk for developing breast cancer. Analysis will include but not be limited to: risk factors for developing breast cancer, effectiveness of various modalities of treatment, and actual risk of developing cancer.

This is a prospective database for patients who are seen in the CBCP Risk Reduction clinic, who have an increased risk of developing breast cancer based on a computerized analysis of their individual risk factors.

### TECHNICAL APPROACH

Patients being seen in the Comprehensive Breast Center at WRAMC will be assessed for their risk of developing breast cancer by their history of LCIS or by applying the Gail Model. Identified high risk patients will be referred to the Clinical Breast Care Project's (CBCP) Risk Reduction Clinic. If the patients are confirmed to meet the inclusion criteria and sign a consent form, they will be enrolled into this study and included in the database.

An amendment finally approved 23 October 2001 updated the initial and follow-up study questionnaires to include several additional items for both the patient and provider to complete. These are questions related to stress, caffeine intake, and geographic residency. The consent form was also modified to inform respondents of the additional time required to complete the questionnaire.

### PRIOR AND CURRENT PROGRESS

The number of subjects enrolled to the study since last APR at WRAMC is 64 and the total enrolled to date at WRAMC is 140.

### CONCLUSIONS

Surgical and medical oncology, specifically with regards to breast cancer, is rapidly advancing as the science in the realm of carcinoma advances. The identification of high-risk groups and specifically risk factors for the development of breast cancer has and will continue to aid in the early detection and treatment. The creation of a database for all high risk for breast cancer patients at WRAMC is ongoing.



## DETAIL SUMMARY SHEET

TITLE: Comparison of Two Plasminogen Activators in Reducing Bleomycin Induced Pulmonary Fibrosis in the Rat

KEYWORDS: animal, rat, pulmonary fibrosis model, ARDS, hydroxyproline, bleomycin pulmonary injury, fibroproliferation, rtPA, rhUK

PRINCIPAL INVESTIGATOR: Mongan, Paul LTC MC

DEPARTMENT: Surgery  
SERVICE: Anesthesia-Operative

STATUS: O  
INITIAL APPROVAL DATE: 3 October 2000

STUDY OBJECTIVE

To compare and contrast anti-fibrinolytic agents in reducing lung fibrosis using the rat bleomycin lung fibrosis model.

TECHNICAL APPROACH

In the proposed study, a rat bleomycin induced pulmonary fibrosis model as described by Thrall *et al* will be utilized to evaluate to efficacy of transtracheal rtPA and rhUK treatment in reducing lung fibrosis. The extent of lung fibrosis in test animals, as estimated by the lung collagen levels, will be determined from the hydroxyproline content in the rat lungs using a procedure described by Woessner. Lung tissue will also be examined histologically for bleomycin induced fibrotic lesions in control and test animals. Based on the literature, this will be the first study to evaluate the fibrinolytic rtPA as a treatment for lung fibrosis. This research should also provide insight into which fibrinolytic, rtPA, or rhUK, is more effective in reducing bleomycin induced lung fibrosis in the rat model.

The experimental design is a block randomized control study (control injury and therapy) of the effect of the treatments rTPA and rhUK in reducing fibrosis in a rat bleomycin model of ARDS. In brief, sixty adult male Sprague-Dawley rats weighing 240-280 gm will be block randomized into five groups. Twelve rats will serve as the sham injury and control vehicle therapy group (0.3 ml phosphate-buffered saline (PBS) control). The additional forty-eight rats will be subjected to a standard intratracheal bleomycin lung injury protocol and randomized to one of four intratracheal treatments of rTPA (250 or 500 mcg in 0.3 ml PBS), rhUK (12,500IU), or delivery vehicle controls (0.3 ml PBS). On day zero, all rats will be anesthetized with IP pentobarbital Na (50 mg/kg). Using aseptic technique, the ventral neck of the rat will be shaved and disinfected with providone iodine. Following a 0.5 cm midline incision, the trachea will be punctured with a 25-ga needle, and lung injury induced by injection of bleomycin (1.5 units of bleomycin sulfate in 0.3 ml PBS, n=48) or the delivery vehicle (0.3 ml PBS, n=12). Surgical incisions will be closed with 4.0 Vicryl™ tissue adhesive will be used to reinforce all surgical closures. On day twenty, a second intratracheal injection will be performed as described above. Bleomycin injury rats will be randomized to one of four treatments (PBS, rTPA 250 mcg, rTPA 500 mcg, rh UK 12,500 IU). Both the sham injury and control treatment rats will receive PBS following tracheal puncture. These control animals will be representative of "normal" collagen synthesis rates with and without bleomycin injury. On days 23 and 49, six rats from each treatment and control group will be sacrificed with a lethal dose of pentobarbital Na IP. The two study times were selected to determine: 1) if there is an immediate reduction in lung collagen following treatment and 2) if this effect persists. The lung tissue will be evaluated for hydroxyproline content and fibrosis by histopathology.

Lung collagen levels will then be determined from the hydroxyproline content of the tissue as described by Woessner. The right lung on each animal will be dissected free from major bronchi and mediastinal structures and placed in normal saline. The lung tissue will then be homogenized in 2.0 ml of 0.5 M acetic acid and then desiccated overnight. The desiccated right lung will be divided into three 50mg samples and then hydrolyzed in 6N HCL overnight at 110°C. Hydrolyzate will then be neutralized with 2.5M NaOH to a pH of 6-7. Aliquots containing 2 ml of hydrolyzate will then be mixed with 1 ml of chloramine T and allowed to stand for twenty minutes to oxidize hydroxyproline in the sample. The chloramine T is then removed with the addition of 1 mL perchloric acid over a period of five minutes.

#### Work Unit # 01-2001a [Continued]

Finally, color is developed by adding 1 ml of p-dimethylaminobenzaldehyde and placing samples in a 60°C water bath for twenty minutes followed by cooling with tap water for five minutes. Content of hydroxyproline is then determined spectrophotometrically at 557mu. The average of the three 50mg tissue samples will represent the collagen value for that study animal. Collagen content will be expressed as a percent collagen increase above negative PBS controls. Collagen content data will be statistically compared to determine any differences among groups.

On days 23 and 49, after removal of the right lung for hydroxyproline analysis, the left lung will be perfused in situ with PBS followed by 10% buffered formalin. The right lung will then be dissected free and fixed in formalin overnight prior to embedding in paraffin. Paraffin sections will be stained with hematoxylin and eosin and with Mallory trichrome stains. Slides will then be examined by two pathologists blinded to the treatment for amount of interstitial lung collagen in three high power fields which will be expressed as 0=normal, 1=25% lung fibrosis in field, 2=50% fibrosis, 3=75% fibrosis. Observational scores will be used for statistical analysis and compared to the collagen content data.

The sham injury PBS therapy group will serve as the baseline for hydroxyproline and fibrosis analysis (negative control). The bleomycin injury and PBS therapy group will serve as the maximal injury group (positive controls). Data will be referenced to the negative control data and expressed as median with quartiles. The primary outcome analysis will be an evaluation of injury reduction (hydroxyproline content and fibrosis scoring) at 23 and 49 days secondary to rTPA and rhUK. The primary comparison will be to the positive controls. This analysis will be accomplished by a nonparametric two-way analysis of variance between the injury groups with repeated measures over time. The secondary outcomes of interest are the analysis in the progression of fibrosis within the groups (within group difference at day 23 and 49). The differences in fibrosis progression will be compared by an analysis of variance on ranks between the groups.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

None; funding provided by WRAMC through fiscal year 2001 could not administratively be transferred to USUHS in sufficient time to conduct the protocol.

#### CONCLUSIONS

None.

## DETAIL SUMMARY SHEET

**TITLE:** A Prospective, Randomized, Double-Blind, Multicenter Trial Assessing the Safety and Efficacy of Sequential (Intravenous/Oral) BAY 12-8093 (moxifloxacin) 400mg Every 24 Hours Compared to Intravenous Piperacillin/Tazobactam 3.375 grams Every Six Hours Followed by Oral Amoxicillin/Clavulanic Acid Suspension 800 mg Every Twelve Hours for the Treatment of Patients With Complicated Intra-Abdominal Infections

**KEYWORDS:** moxifloxacin, complicated intra-abdominal infections, Piperacillin/Tazobactam, Amoxicillin/Clavulanic Acid

**PRINCIPAL INVESTIGATOR:** MAJ Michael M. Woll, MC

**ASSOCIATES:** LTC George E. Peoples, MC; CPT Jennifer M. Gurney, MC

**DEPARTMENT:** Surgery

**STATUS:** C

**SERVICE:** General Surgery

**INITIAL APPROVAL DATE:** 12 December 2000

### STUDY OBJECTIVE

To prove that sequential IV/Oral Moxifloxacin therapy is not worse than treatment with IV Piperacillin/Tazobactam as an adjunct to surgical treatment of complicated intra-abdominal infections.

### TECHNICAL APPROACH

Patients diagnosed with complicated intra-abdominal infections are screened for inclusion in the study. If they meet the inclusion and exclusion criteria, they are enrolled and undergo either surgical exploration or interventional radiology fluid aspiration. The infected material is split and half is sent to our lab for routine bacteriologic testing and the other half is sent to a central lab (Covance Laboratories, Indianapolis, IN). Once enrolled, patients receive either IV Moxifloxacin 400mg QD or IV Piperacillin/Tazobactam 3.375 grams IV q 6 hours. Blinding is performed by the pharmacy. Switch to oral medications is made when the patient's clinical status allows it. The endpoint is resolution of symptoms. Serial blood chemistry measurements are made at the time on enrollment, day of IV to PO switch, and at the Test of Cure visit (TOC).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 8 and the total enrolled to date at WRAMC is 9. The total number enrolled study-wide is 451 if multi-site study.

### CONCLUSIONS

There has been no interim monitoring by Bayer, and no results have been given to the clinical sites. Therefore, we have no conclusions to date.

## DETAIL SUMMARY SHEET

TITLE: A Prospective Randomized Phase III Study Comparing Radiofrequency Ablation Versus Cryosurgical Ablation for the Treatment of Malignant Liver Tumors

KEYWORDS:

PRINCIPAL INVESTIGATOR: Peoples, George LTC MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: General Surgery

STATUS: C  
INITIAL APPROVAL DATE: 23 January 2001

STUDY OBJECTIVE

To evaluate any differences in morbidity, disease-free survival, or overall survival in patients with metastatic liver cancer treated with ablative technologies.

TECHNICAL APPROACH

After randomization, patients undergo either radiofrequency ablation or cryoablation intra-operatively of liver mets. End points include post-op morbidity and disease-related survival.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Due to poor accrual related to overall number of available patients and surgeons' preference for one of the ablative techniques, we will close this trial.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 2, if multi-site study.

CONCLUSIONS

We may consider re-opening this trial at a later date, but currently the enrollment has been poor.

## DETAIL SUMMARY SHEET

**TITLE:** Comparison of Doppler Flow Characteristics of the Superior Mesenteric Artery to Invasive Pulmonary Artery Catheterization in Critically Ill Patients

**KEYWORDS:** Doppler, SMA blood flow

**PRINCIPAL INVESTIGATOR:** CPT Jimmie Anderson MC

**ASSOCIATES:** LTC Goff

**DEPARTMENT:** Surgery

**SERVICE:** General Surgery

**STATUS:** O

**INITIAL APPROVAL DATE:** 22 May 2001

### STUDY OBJECTIVE

To describe blood flow in critically ill patients using noninvasive duplex ultrasound and pulmonary artery catheter (PAC) measurements. To explore whether changes in hemodynamic status influence resistance index, pulsatility index, SMA diameter and flow using duplex ultrasound. To explore whether a relationship exists between blood flow recorded by duplex ultrasound and blood flow recorded by pulmonary artery catheter. PI anticipates finding a decreased SMA flow during hypovolemic shock.

### TECHNICAL APPROACH

Prospective, nonrandomized, one group, pilot study. Subjects in this study will essentially be used as their own controls because all patients/subjects eligible for study will have both ultrasound and PAC measurements done.

**Methodology:** Subjects will be recruited preoperatively when the use of PAC is anticipated (a probable significant blood loss) or postoperatively if PAC is inserted. The decision for the use of pulmonary artery catheter (PAC) will be made by the primary team. No patient will have a PAC placed or extended for the purpose of this study. Patient will consent prior to elective surgery or in the ICU. Preliminary data will be collected from patient medical records such as sex, age, body mass index, pertinent past medical history, diagnosis, fasting status, and vasoactive drug use. This data will be placed in the database. This data must be collected because it may affect measurements between patients. Patient will be given an ID number. No name, hospital ID, or SSN will be placed in the database. Pertinent past medical history includes diseases that may contribute to false vascular readings such as hypertension, diabetes, peripheral vascular disease, cardiomyopathy, congestive heart failure, mesenteric occlusive disease, renal insufficiency, or hepatic insufficiency. Data will then be collected from all consecutive PAC measurements between the hours of 0500 and 2300 until the sample size has been achieved. Any interventions based on PAC readings will be recorded. Possible interventions include fluid boluses, blood transfusion, antibiotics, vasoactive drug use, or discontinuation. No additional PAC readings for the purpose of the study will be obtained. One of the investigators will perform duplex ultrasound within ten minutes of the PAC measurements, allowing minimal disruption of normal routine. PI will take the ultrasound to the ICU where PI will be performing the ultrasounds. A total of four repeat ultrasound measurements will be taken and recorded in our database. PAC measurements are typically done every four hours. There are exceptions. For example, open hearts are done more frequently. The number of measurements may be less in accordance with the duration of PAC, as judged by the primary care team. For example, a patient who underwent a CABG will require frequent measurements immediately out of the operating room until stabilized; then every 2-4 hours until the following morning. At that time, if the postoperative course was uneventful, the cardiothoracic surgeon discontinues the catheter the next morning. In this example, a measurement will be obtained after the patient is moved to the ICU, then again if a change in hemodynamic parameters occurred during the initial stabilization period, and then again every 2-4 hours when repeat pulmonary artery catheter measurements are obtained...until the catheter is discontinued or a maximum of four measurements are obtained. Each study will take approximately 10-15 minutes. Possible limitations include obesity, overlying bowel gas, and recent abdominal surgery. Thin body

habitus, no abdominal incision, and great experience should be associated with faster scanning times. A completion ultrasound will be obtained after the pulmonary artery catheter is discontinued. The use of ultrasound in this study will have no impact on clinical decisions.

**Data Collection:** Patient information collected on data sheet will include sex, age, body mass index, pertinent medical history, diagnosis, fasting status, and use of vasoactive agents. In addition, pertinent labs to include any lactate level, arterial blood gas, and hemoglobin measurements will be documented that corresponds to a particular measurement. No additional labs will be ordered for this study; only existing lab data will be used. Cardiac output, cardiac index, systemic vascular resistance, pulmonary artery pressure, mean arterial blood pressure, stroke volume, central venous pressure, mixed venous saturation, and heart rate will be collected from the pulmonary artery catheter measurements and entered in our database. Corresponding ultrasound measurements to include pulsivity index, resistance index, SMA diameter, and systolic and diastolic flow velocities from four encounters will also be entered into the database. SMA flow will be calculated.

**Sample Size/Data Analysis:** This pilot study will contain a total of twelve in the study sample (ten subjects determined a priori sample size plus two subjects to account for missing data or dropouts). Permission is requested to enroll up to 25 subjects in order to obtain the total sample size. Descriptive statistics will be presented for all demographic variables, pulmonary artery catheter measurements, and SMA duplex measurements. Where appropriate, bar graphs, line graphs, and “box-n-whisker” plots will be presented for study variables. PI will keep track of how many decided not to participate in the study and the reason for non-participation, if known. Given the descriptive statistics that will be reported here, an interesting and related question is the following: To what extent do the data for each outcome variable resemble a normal distribution? An answer to this question may assist the PI in the future development of a clinical trial by suggesting which outcome variables to include in a future study. For the continuous data collected in the study, the nonparametric, Kolmogorov-Smirnov (K-S) one-sample test is useful to evaluate the null hypothesis that the cumulative distribution of a cardiac output (and separately for each multiple measurement) is similar to that of a normal distribution. For nominal, dichotomous data (e.g. gender), the nonparametric, binomial test will be used to evaluate a similar null hypothesis. For nominal data with multiple levels, (e.g. race), the nonparametric, chi-square goodness-of-fit test will be used to evaluate a similar null hypothesis. All tests will be two-tailed, and SPSS will be the statistical software package used in data analysis.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No recent changes in the literature. No results available for analysis. The number of subjects enrolled to the study since last APR at WRAMC is 0. The total enrolled to date at WRAMC is 0.

#### CONCLUSIONS

No results available for analysis.

## DETAIL SUMMARY SHEET

TITLE: Tissue and Blood Library Establishment for Molecular, Biochemical, and Histologic Study of Breast Disease

PRINCIPAL INVESTIGATOR: COL Craig Shriver MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: General Surgery

INITIAL APPROVAL DATE: 22 May 2001

### STUDY OBJECTIVE

1. Acquisition and banking of breast tissue, lymph nodes and/or blood from informed and consenting donors.
2. Experimental analysis of DNA, RNA, and/or proteins isolated from donor tissues for molecular, biochemical, immunological and/or histopathological analysis.
3. Establishment of an integrated and relational database for tissue/serum and patient clinical characteristics that will provide the resources necessary to achieve the following future goals:
  - a. Identify single nucleotide polymorphisms (SNPs) present in DNA from diseased breast tissue (as defined by histologic criteria) as compared to breast tissue without disease, lymph nodes with and without metastatic deposits, and/or DNA derived from patient leucocytes.
  - b. Identify differences in RNA and protein expression associated with breast disease (as defined by histologic criteria) as compared to normal breast tissue and lymph nodes with and without metastatic deposits.
  - c. Correlate SNPs and differences in RNA and protein expression associated with diseased breast and nodal tissue (as defined by histologic criteria) with the corresponding clinical patient database.
  - d. Identify factors within patient serum and/or blood-derived cellular components that correlate with patient risk factors or clinical status as defined in the corresponding clinical patient database.

### TECHNICAL APPROACH

**Methodology:** The approach to collection of the samples to be achieved is as follows, based on the grouping of the patients presenting (corresponding to the subjects groups in section 9a above). Patients already diagnosed with breast cancer: This group will consist of patients who already have undergone a breast biopsy of any type, at WRAMC or another institution (after confirmation of the pathology diagnosis at that other institution), which has confirmed a cancer diagnosis that requires further surgical therapy as per the consensus recommendation of the multidisciplinary breast conference. Approximately 8cc of blood will be obtained from a peripheral venous access line that has been placed for the administration of anesthetic or fluids. Once the breast tissue is surgically removed, as clinically indicated, the specimen(s) will be taken to the pathology laboratory where a licensed pathologist will ensure that the tissue is adequate for routine pathology analyses (diagnosis, margin status assessment, and other indicated purposes). If appropriate, an FNA (fine needle aspiration) utilizing a 22 gauge needle/syringe setup will be performed on the breast and/or lymph node specimen(s), and the cytologic contents placed in standard solution, centrifuged, and flash frozen prior to placing them in the freezer. Then, and only then, if any actual excess tissue (cancerous or benign) remains, samples of that tissue will be harvested for archiving in the tissue bank. This archival tissue will be divided and placed into vials, labeled with code number after all patient identifiers are removed, and flash-frozen in liquid nitrogen. It will then be placed into the CBCP Tissue Bank freezer at temperatures down to -180°C. Blood samples will be centrifuged prior to separation and flash freezing of the serum and non-serum contents, and placed into the -180°C freezer. This tissue will remain in the freezer at the WRAMC site for at least a two-week period of time, or longer if needed. During this time, no analyses will be performed on the specimen – this period of time will be known as the “Fail-Safe” time period. The Fail-Safe time period is intended to allow the diagnostic testing they determine is necessary to patient care. After the pathologist determines with final certainty, by the publishing of the official final pathologic report with no outstanding addenda, that there is no diagnostic pathologic requirement for the frozen specimen(s) on that patient (identified only by code with the logbook as noted above) will be released to the CBCP for research analyses. This will include transfer of the tissues to offsite locations for specialized studies (to include functional genomics, proteomics, and immunologic analyses). The serum and non-serum contents of the blood will, after appropriate labeling and removal of all patient identifiers,

linked only to the patient via the codebook, be either held in the freezer indefinitely or transferred to one of the CBCP offsite research facilities for immunologic or proteomic analysis. The cytologic aspirate will likewise, after appropriate labeling and removal of all patient identifiers, linked only to the patient via the codebook, be either held in the freezer indefinitely or transferred to one of the CBCP offsite research facilities for molecular, proteomic, immunologic, and/or histopathologic analysis. All consenting adult patients presenting to the Breast Center or the Women's Imaging Center at WRAMC with evidence of breast disease for which a breast tissue biopsy (to include ductal lavage, open breast biopsy, tru-cut biopsy, image-directed biopsy) is clinically indicated. After consent is obtained, patients will fill out the standard questionnaire and then be taken to procedure or surgery. Approximately 8cc of blood will be obtained from a peripheral venous access line that has been placed for the administration of anesthetic or fluids. If no IV access is clinically indicated, consenting patients will have the blood drawn using standard sterile techniques from a peripheral vein. Once the breast tissue is surgically removed, as clinically indicated, the specimen(s) will be taken to the pathology laboratory analyses (diagnostic, margin status assessment, and other indicated purposes). If deemed appropriate, an FNA utilizing a 22-gauge needle/syringe setup will be performed on the specimen, and the cytologic contents placed in standard solution, centrifuged, and flash frozen prior to placing them in the freezer. To clarify, this will be on a specimen already removed from the patient, now in the hands of the pathologist, who will take a 22-gauge or equivalent needle on a syringe and make several passes into the biopsy specimen in order to retrieve and store individual cells (cytology) that in no way will negatively affect the actual standard pathologic analysis. Then, and only then, if any actual excess tissue (cancerous or benign) remains, samples of that tissue will be harvested for tissue archiving in the tissue bank. This archival tissue will be divided and placed into vials, labeled with a code number after all patient identifiers are removed, and flash-frozen in liquid nitrogen; it will then be placed into the CBCP Tissue Bank freezer at temperatures down to -180°C. Blood samples will be centrifuged prior to separation and flash freezing of the serum and non-serum contents, and storage at -180°C. This tissue will remain in the freezer at the WRAMC site for at least a two week period of time, or longer if needed, where no analyses will be allowed to be performed on it – this period will be known as the “Fail-Safe” time period. The intent of the fail-safe time period is to allow the diagnostic pathologists to request that the banked tissue be brought back out of freezer and thawed for diagnostic testing if it is determined to be necessary for any reason. After the pathologist determines with final certainty, by the publishing of the official final pathologic report with no outstanding addenda, that there is no diagnostic pathologic requirement for the frozen specimen(s), then the archived specimen(s) on that patient (identified only by code with the logbook as noted above) will be released to the CBCP for research analyses. This will include transfer of the tissues to offsite locations for specialized studies (to include functional genomics, proteomics, and immunologic analyses). The serum and non-serum contents of the blood will, after appropriate labeling and removal of all patient identifiers, linked only by the patient via the codebook, be either held in the freezer indefinitely or transferred to one of the CBCP offsite research facilities for molecular, immunologic biochemical, histological, and/or proteomic analysis. The cytologic aspirate will likewise, after appropriate labeling and removal of all patient identifiers, linked only to the patient via the codebook, be either held in the freezer indefinitely or transferred to one of the CBCP offsite research facilities for immunologic or proteomic analysis. All consenting adult patients presenting to the WRAMC plastic surgery clinic for elective reductive mammoplasty are screened by routine clinical measures of mammography (if indicated) and clinical breast examination. If they are found to have no contra-indication to said procedure, have been appropriately counseled by a licensed Plastic or General Surgeon, and if they are patients who still desire elective reduction mammoplasty, consent is obtained, patients will fill out the standard questionnaire, and are taken to surgery. Approximately 8cc of blood will be obtained from a peripheral venous access line that has been placed for the administration of anesthetic or fluids. Once the breast tissue is surgically removed, as clinically indicated, the specimen(s) will be taken to the pathology laboratory where a licensed pathologist will ensure that the tissue is adequate for routine pathology analyses (diagnosis, margin status assessment, and other indicated purposes). If appropriate, an FNA (fine needle aspiration) utilizing a 22-gauge needle/syringe setup will be performed on the breast and/or lymph node specimen(s), and the cytologic contents placed in standard solution, centrifuged, and flash frozen prior to placing them in the freezer. Then, and only then, if any actual excess tissue (cancerous or benign) remains, samples of that tissue will be harvested for archiving in the tissue bank. This archival tissue will be divided and placed into vials, labeled with a code number after all patient identifiers are removed, and flash-frozen in liquid nitrogen. It will then be placed into the CBCP Tissue Bank freezer at temperatures down to -180°C. Blood samples will be centrifuged prior to separation and flash freezing of the serum and non-serum contents, and placed into the -180°C freezer. This tissue will remain in the freezer at the WRAMC site for at least a two weeks, or longer if needed, where no analyses will be allowed to be performed on it. This period will be known as the “Fail-Safe” time



period. After the pathologist determines with final certainty that there is no diagnostic pathologic requirement for the frozen specimen(s), the archived specimen(s) on that patient will be released to the CBCP for research analyses. This will include transfer of the tissues to offsite locations for specialized studies (to include functional genomics, proteomics, immunologic, and histopathologic analyses).

The serum and non-serum contents of the blood will, after appropriate labeling and removal of all patient identifiers, linked only by to the patient via the codebook, be either held in the freezer indefinitely or transferred to one of the CBCP offsite research facilities for functional genomics, proteomics, and/or immunologic analysis. Primary uses of the tissue and serum specimens: The known primary uses under this protocol for the acquired tissues and serums/blood fall into seven major subsections. These are:

Tissue Banking  
BioImaging/Microscopy  
Gene Expression Profiling  
Sequencing

Genotyping  
Pharmacogenomics  
Protein Expression Profiling

At the end of each of the above seven laboratory workflows, the data will be QA'd, analyzed using powerful genomics/proteomics software tools, and placed into the CBCP database/data warehouse. QA of the data involves using software tools that interrogate the fields of the data that come out of the workflow stations. This is to ensure the data has consistency, and is within expected or known ranges. Any data found to be outside of expected ranges is not necessarily flawed but is then identified for closer analysis by researchers.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

An Addendum dated 11 June 2002 requested an increase of "up to 20cc of venous blood" be collected for the collection of plasma for additional molecular studies. The Human Use approved the addendum on 10 July 2002. There have been no adverse events with this minimal risk protocol and no patients have withdrawn from the study. The number of subjects enrolled to the study since last APR at WRAMC is 430 and the total enrolled to date at WRAMC is 663. The total number enrolled study-wide is 733, as a multi-site study (Windber). A review of the literature revealed no publications within the last year reporting data from studies of a similar design.

#### CONCLUSIONS

The study is ongoing.

## DETAIL SUMMARY SHEET

TITLE: Creation of a Blood Library for the Analysis of Blood for Molecular Changes Associated with Breast Disease and Breast Cancer Development

PRINCIPAL INVESTIGATOR: LTC Craig Shriver MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: General Surgery

INITIAL APPROVAL DATE: 22 May 2001

### STUDY OBJECTIVE

1. Acquire and bank blood serum from informed and consenting donors.
2. Characterize gene and protein expression profiles and single nucleotide polymorphisms associated with breast disease and breast cancer development.
3. Identify factors within patient serum and/or blood-derived cellular components that correlate with patient risk factors or clinical status as defined in the corresponding clinical patient database.

### TECHNICAL APPROACH

Methodology: Blood collection and processing workflows: Patients will be categorized into the appropriate groups and about 8-12 ml of venous blood collected by a phlebotomist or nurse. Before blood draw, the PI or designee would provide a consent form and explain the study to the patient. The patient will sign the consent form if willing to participate. All consenting patients will be assigned a unique CBCP identification number, which will not reveal patient identity. The blood will be drawn and a portion of it placed in PAX-gene blood tubes (Qiagen, Inc.), which stabilizes the RNA for up to seven days. Plasma and serum will be processed within two hours by spinning blood down and aliquoting into separate tubes, after which they will be stored in the CBCP laboratory freezer. On a weekly scheduled basis, samples will be transferred to the CBCP Genomics/Proteomics Center at the Windber Research Institute where the following procedures will be carried out: RNA, DNA and Protein from blood isolation from blood: RNA will be purified from blood collected in PAXgene RNA tubes using the RNA Test Kit (PAXgene™, Qiagen Inc., CA). RNA will then be employed for other down stream analysis after determining concentration with a DNA/RNA calculator. DNA will be isolated from blood using the QIAamp DNA blood kit. This involves lysing the blood in appropriate buffer and loading this on a spin column. DNA gets bound to the silica gel-based membrane and pure DNA eluted in water or low-salt buffer. Protein will be isolated from plasma or serum samples using an extraction buffer (50mM Tris HCL, pH 7.5 and 0.1% Nonidet P-40) as described below. Approximately two volumes of buffer per volume of the sample are centrifuged at 14,000rpm/15minutes at room temperature. The supernatant is transferred to a fresh tube and about twice its volume of isopropanol added. The mixture is allowed to stand at room temperature for 15-20 minutes before centrifugation as described above. The supernatant is discarded and precipitate reconstituted in the Tris buffer. Total protein concentration will be determined by the Bradford protein assay procedure.

Primary uses of the blood and serum specimens: The known primary uses under this protocol for the acquired serum and blood fall into six major subsections:

1. Serum/Blood Repository Banking – this includes sample definition and receiving, flash freezing/labeling/storage, OCT embedding (placing the blood cells in a special preservative that protects the RNA/DNA during prolonged freezing), labeling (putting identifier codes on each tissue sample for subsequent tracking), storage, and inventory/tracking. The inventory and tracking of all samples will be done electronically with barcodes and sample tracking software – initially the software will be Freezerworks™ to be followed by our own developed software module by Cimarron Inc. that will be integrated with our laboratory analysis software GenoMax™.

2. Gene Expression Profiling – blood samples will undergo RNA isolation by Northern Analysis and RT-PCR, and mRNA selection by RT-PCR, subsequent cDNA synthesis and cDNA Library construction, DNA spotting, hybridization and array scanning, image processing and data analysis, for eventual gene expression profile identification.
3. Sequencing – after plasmid isolation, DNA will undergo PCR setup, thermal cycling, PCR clean-up, capillary electrophoresis, and Sequence Analysis.
4. Genotyping – blood will undergo DNA quantification followed by PCR set-up, thermal cycling, SNP (single nucleotide polymorphism) reaction clean-up, capillary electrophoresis set-up, genotype calling, and genotype QC.
5. Pharmacogenomics – blood will undergo RNA isolation, mRNA selection, cDNA synthesis, probe labeling, probe clean-up, probe fragmentation, suppression hybridization, array scanning, image processing, data analysis, and gene expression profile identification.
6. Protein Expression Profiling – after sample clean up, serum and blood will undergo 1D- and 2D-Electrophoresis, Gel staining, Image acquisition and processing and analysis, and Gene expression Profile identification.

At the end of each of the above seven laboratory workflows, the data will be QA'd, analyzed using powerful genomics/proteomics software tools, and placed into the CBCP database/data warehouse. Any data found to be outside of expected ranges is not necessarily flawed, but is then identified for closer analysis by researchers. Data will be stored in the CBCP server(s) and/or data warehouse (being developed with NCR Inc.), initially on CBCP sites at WRAMC, USUHS, or WRI, and eventually at the CBCP Data Warehouse in Fort Detrick, MD (as part of our MANVT initiative, funded separately). The MANVT initiative allows for the near-real time interaction between all of the four main CBCP sites (WRAMC, USU, Windber network) that would link all of the sites, as well as allow for creation of a data warehouse (situated at least in part at Fort Detrick, MD, or to have a significant redundancy backup there).

Further information regarding various techniques to be used in the above workflows: Molecular analysis of blood: DNA and RNA isolated from the blood samples will be used for other down stream processes such as polymerase chain reaction (PCR) amplification using gene specific primers targeting mutant specific alleles of genes of interest, and quantitative RT-PCR (qRT-PCR) for assessment of the transcriptional profiles of specific genes. Proteins in all samples of the different patient categories will be displayed and identified using 2D-DIGE technologies. Altered proteins will be isolated and sequenced using MALDI/TOF and/or LS-MS-MS and the relevant genes/proteins identified in the human genome sequence database. Disease specific changes will be characterized at the DNA level by cloning, sequencing, and analysis of the genes and regulatory elements. The genomic DNA of patients will be analyzed to determine changes that may have occurred during disease progression or those present only in particular categories of patients as compared to controls. The expression patterns of 500-1000 genes associated with biochemical processes implicated in cancer will be monitored in parallel using microarray technology. The genes being arrayed will include known specific genes implicated in the development of breast cancer, as well as generalized genes (cell cycle regulators, protein shuttle genes, stress-related genes) that conceivably are involved in oncogenic pathways. Briefly, complementary DNA (cDNA) clones representing genes of interest will be spotted on microscopic glass slides and hybridized with differentially labeled cDNA populations synthesized from mRNAs. Such changes would identify potential markers or provide disease specific targets for treatment. Single nucleotide polymorphisms (SNPs) of known gene variants located in coding regions of genes of interest and variants that cause amino acid changes will be characterized. SNPs linked with breast cancer will be identified and then used as diagnostic and predictive markers.

Immunoassays: Quantitative measurement of protein levels in plasma or serum will be carried out using ELISA kits (R & D Systems Inc., Minneapolis, MN). Active and total protein will be measured by an activity assay (e.g. AP Biotrak, Amersham Pharmacia Biotech, Piscataway, NJ). All procedures will be as per manufacturer instructions.

SDS-Page: SDS-Page will be carried out using the Phastgel System (Amersham Pharmacia Biotech, Piscataway, NJ). The procedure involves adding 3µl of loading buffer (950µl Bio-Rad Laemmli sample buffer and 50µl β-mercaptoethanol) to the protein sample, incubating at 95°C for five minutes, snap cooling on ice before separation on 12.5% homogenous or 10-25% gradient gel. Molecular weight markers and known control samples will be electrophoresed simultaneously as positive and negative controls.

Western blot/analysis: Electrophoresed proteins will be transferred into nitrocellulose membrane using the Phast System followed by western analysis using the Western Light Plus Protein detection kit (Tropix Inc., MA) and specific primary antibodies. Blots will be exposed to radiographic films (Kodak Biomax) and presence of protein identified by signals captured on the radiographic films. Signals will be digitized and quantified.

Statistical analysis: Data obtained from the above laboratory analysis will be collated and statistically analyzed. Primary analysis will be comparison of gene and protein expression pattern across the different patient categories.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

An Addendum dated 11 June 2002 requested an increase of “up to 20cc of venous blood” be collected for the collection of plasma for additional molecular studies. The Human Use Committee approved the addendum on 10 July 2002. There have been no adverse events with this minimal risk protocol and no patients have withdrawn from the study. The number of subjects enrolled to the study since last APR at WRAMC is 140 and the total enrolled to date at WRAMC is 280. The total number enrolled study-wide is 397, as a multi-site study (Windber). A review of the literature revealed no publications within the last year reporting data from studies of a similar design.

#### CONCLUSIONS

The study is ongoing.

## DETAIL SUMMARY SHEET

**TITLE:** Percutaneous Arterial Closure After Diagnostic and Interventional Endovascular Procedures - A Prospective Randomized Evaluation of the Perclose Device in Patients with Peripheral Vascular Disease

**KEYWORDS:** Suture Mediated Closure Device, Peripheral Vascular Disease

**PRINCIPAL INVESTIGATOR:** Starnes, Benjamin W. MAJ MC

**ASSOCIATES:** O'Donnell, Gillespie, Goff, Rosa, Chang

**DEPARTMENT:** Surgery

**STATUS:** O

**SERVICE:** Peripheral Vascular Surgery

**INITIAL APPROVAL DATE:** 24 October 2000

### STUDY OBJECTIVE

1. To evaluate the complication rate comparing percutaneous closure versus manual compression in patients with peripheral vascular disease at a single institution.
2. To assess with Color-Flow Duplex Ultrasonography the effects (change in vessel diameter or peak systolic velocity) on the common femoral artery after suture-mediated percutaneous closure in patients with peripheral vascular disease.
3. To determine if sheath size has a positive or negative effect on successful outcome of the suture-mediated percutaneous closure device in patients with peripheral vascular disease.
4. To assess time to hemostasis, time to ambulation and length of stay after suture-mediated N percutaneous closure following diagnostic or interventional arteriography.
5. To assess technical limitations, if any, associated with a suture-mediated percutaneous closure device used specifically in patients with peripheral vascular disease.

### TECHNICAL APPROACH

This study will be a prospective randomized control trial comparing a novel percutaneous suture-mediated closure device with the conventional method of manual pressure. Patients will be divided into those undergoing only diagnostic arteriogram ("D") vs. those undergoing diagnostic arteriogram followed by intervention ("I"). These patients will have the identifier "D" or "I" associated with their case. At the end of each procedure, the patient will be randomized to receive either device "+" or manual compression "-". The only modification is that we will no longer be randomizing patients to the diagnostic arteriogram group due to the device use for those procedures being replaced with the next generation device.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since the last annual report there have been a number of publications on the Perclose device. Most have shown it to be a safe device even with multiple procedures through the same artery. There are several reports of severe infections. We have not seen this in our study group. There have been no adverse occurrences other than the same complications that occur without the device (manual compression).

The number of subjects enrolled to the study since last APR at WRAMC is 18 and the total enrolled to date at WRAMC is 102.

### CONCLUSIONS

Review of the data to date reveal the use of suture mediated closure devices to shorten the length of stay with the same morbidity as the gold standard. With the discontinuation of the 6 French device we would like to continue the study only for the endograft AAA patients and patients requiring large sheaths for other endovascular interventions.

## DETAIL SUMMARY SHEET

TITLE: Telemedical Examination of Eyelid Lesions - Correlation of Remote Diagnosis With In-Person Clinical Exam and Pathologic Analysis

KEYWORDS:

PRINCIPAL INVESTIGATOR: CPT Melvin Wagner MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Ophthalmology

STATUS: O  
INITIAL APPROVAL DATE: 3 April 2001

### STUDY OBJECTIVE:

The purpose of this study is to compare the diagnostic accuracy of remote video examination of eyelid lesions with live exams and final pathologic diagnosis.

### TECHNICAL APPROACH:

Patients presenting to the Ophthalmology Service desiring removal of an eyelid lesion will either be examined by video or in-person analysis after reading and signing the informed consent. The investigators will randomize the subjects to either sequence A (in-person exam followed by video exam) or sequence B (video exam followed by an in-person exam). The sham controls who refuse biopsy of their eyelid lesion but agree to participate in the video portion of the study (denoted sequence C) will have a video of their eyelid lesion. The video examination includes four static images. The video exam of the eyelid is performed using a three dimensional camera.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 3. The total enrolled to date at WRAMC is 18.

### CONCLUSIONS:

We are currently actively enrolling patients into this study with a goal of seventy patients. A smaller than expected number of patients was enrolled over the past year due to a change in the PI resulting from Dr. Weichel's PCS. In addition, there has been some reorganization within the Ophthalmology Service requiring some of the necessary equipment to be moved from one location to another. This problem has been resolved since the new PI has acquired a key to the office containing the aforementioned equipment.

## DETAIL SUMMARY SHEET

**TITLE:** Night Vision Goggle and Night Firing Range Performance After Myopic Excimer Laser Keratorefractive Surgery in U.S. Army Personnel

**KEYWORDS:** Refractive surgery, laser, excimer laser, lamellar, photorefractive keratectomy, contrast sensitivity, visual performance, night vision, night vision goggles

**PRINCIPAL INVESTIGATOR:** Bower, Kraig LTC MC  
**ASSOCIATES:**

**DEPARTMENT:** Surgery  
**SERVICE:** Ophthalmology

**STATUS:** O  
**INITIAL APPROVAL DATE:** 21 November 2000  
**MASTER PROTOCOL APPROVAL DATE:** 20 April 1999

### STUDY OBJECTIVE

- Evaluate visual performance in Night Vision Goggles (NVG) before and after excimer laser refractive surgery. Performance measurements will include high and low contrast targets viewed with and without optical correction.
- Determine the safety of LASIK and PRK in terms of maintenance of best-corrected NVG visual resolution of both high and low contrast targets under a full range of night sky conditions. The magnitude and duration of any transient post-operative changes in best-corrected NVG performance will be evaluated.
- Evaluate the efficacy of PRK and LASIK by assessing improvement of uncorrected NVG visual performance.
- Evaluate whether any measured post-operative NVG performance changes affect the ability to perform a specific task, as determined by performance testing on the night firing range before and after excimer laser refractive surgery.
- Evaluate subjective responses to the surgery to determine satisfaction and complaints with respect to glare, night vision, and halos.

### TECHNICAL APPROACH

This study is an observational-only, non-intervention sub-protocol to the Master Protocol (WRAMC WU#2335-99; HSRRB Log # A-10105.0). It is a two-year, prospective, non-randomized investigation of night vision goggle and night firing performance using a three-group (PRK surgical treatment, LASIK surgical treatment, or no surgical treatment) longitudinal design with measurements taken at four points in time (initial or month 0, and months 1, 3, and 9 after the initial measures). The initial, baseline measures (obtained pre-operative as part of the master protocol for the surgically-treated subjects and abstracted from the master protocol database, and at the initial data collection for control subjects) will consist of a one time only measure of the key variables. The subsequent measures will consist of 3 evaluations made at 1, 3, and 9 months following the surgical procedure or, for the control group, following the baseline measures. The NVG measures specific to this protocol will be made at baseline and at 1, 3 and 9 months post- baseline. All baseline pre-operative evaluation and all study follow-up evaluations will be conducted at Walter Reed, except for NVG acuity and night firing to be conducted at the Night Vision Laboratory, Fort Belvoir. The specific goal of this NVG sub-study is to evaluate the effect of two types of refractive surgery on performance with night vision goggles and the M-16 on the night firing range over time as compared to no surgical intervention.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A total of 20 subjects have enrolled in the NVG sub-protocol to date. Eight have undergone uncomplicated PRK and another 12 uncomplicated PRK. Most have followed up through their 3 month postop visit at the Center for Refractive Surgery for visual performance measures and at the Night Vision laboratory for NVG testing and Night Firing Range performance. There have been no adverse events related to the procedures or the protocol testing. Enrollment has slowed of late due to deployment issues and subject availability as a result of the build up for the war

effort, and we are holding off on enrolling new subjects until such time as we can confirm their availability for the necessary follow-up as specified in the protocol.

The number of subjects enrolled to the study since last APR at WRAMC is 20 and the total enrolled to date at WRAMC is 20. The total number enrolled study-wide is N/A, if multi-site study.

CONCLUSIONS

We are nearly one half of the way toward our enrollment goal for PRK (12 of 25) and one third of our LASIK goal (8 of 25). Post-op follow-up and visual performance testing has been performed on the majority of patients at the one and three month postop interval in the Center for Refractive Surgery and at the Night Vision Laboratory (NVL) and Night Firing Range (NFR).

Clinical results so far show uncorrected visual acuity (UCVA) of 20/20 or better in 19/24 (79.1%) of PRK eyes and 14/16 (81.3%) of LASIK eyes. UCVA was 20/25 or better in 22/24 (91.7%) of PRK eyes and 16/16 (100%) of LASIK eyes. UCVA was 20/40 or better in all eyes treated. Postoperative best spectacle corrected visual acuity (BSCVA) was within one line of the pre-op BSCVA in all eyes. No treatment resulted in a loss of 2 or more lines BSCVA. There were no surgical or postoperative complications in the PRK group.

In the LASIK group, one patient had bilateral epithelial defects during surgery. He was placed in a bandage contact lens and followed closely postoperatively. On post-op day #4 he developed Stage 2 diffuse lamellar keratitis (DLK) and was started on aggressive topical steroid therapy every hour while awake. The following day he had progressed to stage 3 DLK and his LASIK flap was re-lifted and irrigated. After re-floating the flap, he was continued on Q1hr topical steroids. The DLK subsequently resolved, but his flap had microstriae after the initial re-float, and he underwent a second re-float to treat the microstriae. He looked great at the one-month post-op visit and at 3 months post-op, off of all meds, he sees 20/20 and retains BSCVA in both eyes.

Preliminary results from the NVL and NFR have not yet been analyzed. We have not yet tested our control group. So far, clinical results have met or exceeded those published previously, with no major adverse outcomes. The one LASIK patient with the rocky course had a well-recognized post-op complication, and was managed according to the existing standard of care with good results. His long-term prognosis is very good. The primary difficulty with the study right now is the logistical difficulty in getting subjects enrolled, treated, and followed per the protocol, in large part due to the current operational involvement of our study population in the current war on terrorism and the buildup to the war effort in Iraq. Once the military and political climate permits, we will continue/resume enrollment and treatment of subjects until our enrollment goals are met.



## DETAIL SUMMARY SHEET

TITLE: Prospective Evaluation of Keratorefractive Surgery in Army Aviator Trainee

KEYWORDS: Refractive surgery, laser, excimer laser, lamellar, photorefractive keratectomy, contrast sensitivity, flight performance, pilot performance, night vision goggles, night flight

PRINCIPAL INVESTIGATOR: LTC Kraig Bower MC  
ASSOCIATES: LTC Jeff Rabin, LTC Corina van de Pol

DEPARTMENT: Surgery  
SERVICE: Ophthalmology

STATUS: O  
INITIAL APPROVAL DATE: 25 September 2001  
MASTER PROTOCOL APPROVAL DATE: 20 April 1999

### STUDY OBJECTIVE

- Conduct a prospective evaluation of the efficacy and safety of refractive surgery (photorefractive keratectomy or PRK; laser in-situ keratomileusis or LASIK) in Army helicopter pilot trainees.
- Compare flight and visual performance of two keratorefractive surgical treatment modes in pilot trainees: PRK and LASIK.
- Identify factors which predict performance and/or compromise safety during flight training by evaluating the following variables prospectively: mode of refractive surgery, initial refractive error, degree of astigmatism, corneal thickness, pupil size (normal and low light), initial level of visual performance (visual acuity, contrast sensitivity, night vision goggle resolution) under simulated day and night conditions.
- Make formal recommendations on the efficacy and safety of keratorefractive laser surgery for Army aviator training, to include selection criteria and mode of treatment, to achieve optimal flight and visual performance and maximum safety.

### TECHNICAL APPROACH

This sub-protocol is a two-year prospective study of the efficacy and safety of keratorefractive surgery in Army helicopter pilot trainees. Two treatment modes (PRK and LASIK) and a control group will be utilized. If the subject meets FDME vision standards at 1 month post-operative (uncorrected visual acuity of 20/50 or better in each eye, corrected visual acuity of 20/20 or better in each eye, not more than -0.75 D in any meridian, and no complications), then IERW training will commence at a time no sooner than three months post-operative pending the granting of an Exception to Policy and acceptance into the IERW program. Pre- and post-operative visual and flight performance parameters will be measured.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No subjects have been enrolled since approval of this protocol by the WRAMC CIC and HUC. HSRRB at Ft. Detrick has required numerous additional revisions and those have not yet been implemented. Once the final revisions are accepted by HSRB, we will await approval letter to formally begin enrollment.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

We will submit the required revisions to HSRRB and plan to proceed with the study as planned upon approval.

## DETAIL SUMMARY SHEET

TITLE: Operational Assessment of Refractive Surgery for Rated Army Aviators - A Prospective Evaluation

KEYWORDS: Refractive surgery, laser, excimer laser, lamellar, photorefractive keratectomy, contrast sensitivity, flight performance, pilot performance, night vision goggles, night flight

PRINCIPAL INVESTIGATOR: LTC Kraig Bower MC

DEPARTMENT: Surgery  
SERVICE: Ophthalmology

STATUS: O  
INITIAL APPROVAL DATE: 25 September 2001  
MASTER PROTOCOL APPROVAL DATE: 20 April 1999

### STUDY OBJECTIVE

1. Test the null hypothesis that refractive surgery does not significantly impact visual or flight performance of experienced Active Army Aviators by conducting a prospective evaluation of the military occupational-specific impact of photorefractive keratectomy (PRK) and laser in-situ keratomileusis (LASIK) on both visual and flight performance of experienced Active Army Aviators.
2. Identify vision-related pre-operative factors (e.g., initial refractive error, degree of astigmatism, wave front aberrations, corneal curvature or thickness, pupil size, initial level of visual performance) that may predict performance and/or compromise safety of flight.
3. Make formal recommendations on the efficacy and safety of keratorefractive laser surgery for experienced Army Aviators, to include selection criteria and mode of treatment, which insure optimal flight and visual performance with maximum safety.

### TECHNICAL APPROACH

This protocol is a two-year prospective study of the efficacy and safety of keratorefractive surgery in rated Army Aviators. Forty subjects will undergo PRK and forty subjects who will undergo LASIK. Subjects will be UH-60 pilots who will complete pre- and post-operative visual and detailed flight performance testing at USAARL. At WRAMC, subjects will complete pre-operative and post-operative visual and ocular testing and the keratorefractive procedure. The study will evaluate standard FDA-approved PRK and LASIK procedures to determine whether PRK and/or LASIK are compatible with the Army Aviation environment, and if they are safe and effective for rated Army Aviators.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

As of this report, we have treated a total of 14 patients - 7 PRK and 7 LASIK. There have been no adverse events. There has been considerable high-level interest from the Office of the Surgeon General and from the Army Aviation community to have policy issues addressed as soon as possible regarding refractive surgery in aviators. There is additional fiscal pressure, as there was no new congressional appropriation for FY03 for the continuation of the study. It has been suggested that in light of the above factors, and based on PRK experience with Navy and USAF pilots that the PRK part of the present study be shelved and that the study continue to enroll only LASIK patients. COL Madigan also recommends that an interim report after the 3-6 month post-op evaluation of the first 15 LASIK patients be prepared and forwarded to OTSG by the fall of 2003. The WRAMC PI will consult DCI on the appropriate steps to take.

The number of subjects enrolled to the study since last APR at WRAMC is 14 and the total enrolled to date at WRAMC is 14. The total number enrolled study-wide is N/A, if multi-site study.

### CONCLUSIONS

Consideration must be given to ending the PRK arm of this study and proceeding with the evaluation of LASIK in US Army Aviators. A protocol modification will be submitted after obtaining WRAMC DCI guidance.

## DETAIL SUMMARY SHEET

**TITLE:** Quantitative Analysis of the Neovascularization of Distraction Osteogenesis from the End of Distraction to Bone Maturity Correlated with Bone Histology, Mechanical Properties, and Radiography

**KEYWORDS:** Distraction Osteogenesis, DEXA

**PRINCIPAL INVESTIGATOR:** CPT Roxanne Wallace MC

**ASSOCIATES:** COL Kathleen A. McHale, MC

**DEPARTMENT:** Orthopaedics and Rehabilitation

**STATUS:** C

**SERVICE:** Orthopedics Surgery Service

**INITIAL APPROVAL DATE:** 3 October 2000

### STUDY OBJECTIVE

The capillary density of the distraction gap will increase from zero at the time of osteotomy to that of normal mature bone at the end of consolidation. The radiographic, mechanical, and histological properties at each interval will correlate with the increase in capillary density.

### TECHNICAL APPROACH

No addenda.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study complete; no new animals enrolled in the last year.

### CONCLUSIONS

In the early post-distraction period when cartilaginous or fibrocartilaginous defects interrupt the longitudinal continuity of osseous trabeculae, strength only moderately correlates with density. After these defects ossify, the density-contributing substance is distributed within the material uniformly such that it can distribute stress throughout itself, and strength correlates with density. This is the optimal time period to use DEXA to predict strength. However, once remodeling begins, there is again a non-uniform distribution of osseous trabeculae resulting in no correlation between density and strength.

## DETAIL SUMMARY SHEET

TITLE: Pre-operative and Post-operative EMG Analysis of Rotator Cuff Tears - Clinical Outcome Correlation with MRI Findings, Size and Repairability

KEYWORDS:

PRINCIPAL INVESTIGATOR: Doukas, William LTC MC

ASSOCIATES: Andersen, Romney MAJ MC, Pasquina, Paul MAJ MC

DEPARTMENT: Orthopaedics and Rehabilitation

STATUS: C

SERVICE: Orthopaedic Surgery

INITIAL APPROVAL DATE: 30 November 2000

### STUDY OBJECTIVE

Assess the innervation status of the rotator cuff muscles pre-operatively and post-operatively to see if any change is seen after the repair of the muscles.

### TECHNICAL APPROACH

Test innervation status of suprascapular nerve to rotator cuff muscle before and after rotator cuff repair and compare this with their unaffected side.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The interim results of the study did not support our thesis that a rotator cuff tear would put a strain on the suprascapular nerve thus causing decreased EMG readings. Our study showed that the EMG readings varied widely and that our initial assumption that the sides with the rotator cuff tear would be worse than the unaffected sides was not true. Thus the basis of the study was flawed and it is pointless to continue through to the conclusion of the study.

The number of subjects enrolled to the study to date at WRAMC is 21.

### CONCLUSIONS:

Rotator cuff tears are not well correlated with EMG findings.

## DETAIL SUMMARY SHEET

TITLE: An Observational Study to Record Process Measures and Analyze Cost Related to Iliac Crest Bone Graft Harvest for Spinal Fusion

PRINCIPAL INVESTIGATOR: COL David W. Polly, Jr. MC

ASSOCIATES: LTC Timothy R. Kuklo MD JD, Eileen Bronfman RN MA, CPT Aman Dhawan MD

DEPARTMENT: Orthopaedics and Rehabilitation

STATUS: O

SERVICE: Orthopaedic Surgery

INITIAL APPROVAL DATE: 2 January 2001

### STUDY OBJECTIVE

A prospective, observational study of posterior iliac crest bone harvesting is ongoing using process measures to establish a normative bone harvesting database for future comparative studies and analysis of bone graft substitutes. The objective of the study is to establish a normative data set of the parameters of iliac crest bone graft harvest recording. This will establish a baseline for comparing the use of autologous bone graft to emerging alternatives.

### TECHNICAL APPROACH

Between August 2000 and March 2002, autogenous posterior iliac crest bone graft harvest was obtained from forty patients (31 male and 9 female) under supervision of a fellowship-trained spine surgeon. Bone graft was obtained using the "trephine curettage" technique through a separate incision from the primary surgery. Data collection included estimated blood loss for the procedure and the harvest proper, total time for the harvest, and total bone harvested as measured after packing using a calibrated specimen cup.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Autogenous iliac crest bone graft is currently the "gold standard" when attempting an arthrodesis in various clinical scenarios. In spine surgery, autogenous iliac crest bone graft (ICBG) is one of the most commonly performed procedures because iliac crest is the most common donor site. Various authors have reported the potential dangers, biomechanical consequences, and the associated complications including superficial or deep infection, sensory loss, nerve and/or arterial injury, peritoneal perforation, and sacroiliac instability. The incidence of minor complications ranges from 4% to 20.6%. The incidence of major complications ranges from 0% to 8.6%. Because of this morbidity, bone graft substitutes are emerging. The theoretical advantages include decreased operative time and ease of use with great versatility in size, shape, and volume of graft needed. Economic efficacy and clinical benefit of these substitutes will need to be established before these bone substitutes become standard of care. A critical analysis of both ICBG harvesting and bone graft substitutes is needed. The estimated blood loss for the index procedure averaged 676 cc (range 150-1500 cc). The estimated blood loss for the harvest proper averaged 70 cc (range 20-200 cc). Average harvest time was 36 minutes (range 20-51 minutes) with an average bone harvest volume of 38 cc (range 25-65 cc). The iliac crest bone graft size and sacroiliac joint were clearly visualized in 30 of 40 patients (75%) with one sacroiliac violation (3%). Other than the above, no adverse reactions have been noted.

The number of subjects enrolled to the study since last APR at WRAMC is 26 and the total enrolled to date at WRAMC is 40.

### CONCLUSIONS

Iliac crest bone harvest adds time and contributes blood loss to the index procedure. Average volume of bone harvested during posterior iliac crest bone grafting is 38 cc. These process measures must be taken into consideration in light of the emerging field of bone graft substitutes as they contribute to patient complications and cost.

## DETAIL SUMMARY SHEET

TITLE: Prospective Cohort Analysis of Hip Arthroscopy in Young Active Adults with Two Years Follow-Up.

KEYWORDS: Hip scope, prospective, outcomes

PRINCIPAL INVESTIGATOR: Romney C. Andersen, MAJ MC

ASSOCIATES: Kevin P. Murphy, LTC, MC; Brett A. Freedman, CPT, MC

DEPARTMENT: Orthopaedic Surgery & Rehabilitation

STATUS: O

SERVICE: Orthopaedic Surgery Service

INITIAL APPROVAL DATE: 6 February 2001

### STUDY OBJECTIVE

Assess the results of hip arthroscopy done at Walter Reed Army Medical Center on a prospective basis.

### TECHNICAL APPROACH

This is a prospective clinical trial intended to measure the clinical outcome of hip arthroscopy in the treatment of painful intra-articular hip pathology. There have been no changes to the methods outlined in our approved protocol. Briefly, we will enroll and consent patients on a voluntary basis. Patients will complete validated outcome-based questionnaires pre-op and at each of the planned post-op visits. The response will be coded and statistically analyzed to enable us to report the overall success of this procedure.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been no recent change in the literature. Our research questions remain unanswered. We have not officially enrolled any patients to date and therefore have no results or adverse events to report. No amendments have been made.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

This study has been essentially idle since its inception. As a result of delayed approval and changes in the residency, this worthy project has not moved forward. The four cases reported in 2001 were not complete. They were missing consent forms, questionnaires, or other pertinent information. As a result, this project will be restarted. Brett Freedman will assume the role as principal investigator pending approval of the change. We will restart this project immediately and ensure diligent matriculation and follow-up.

### CONCLUSIONS

This study is still open and no conclusions have been made.

## DETAIL SUMMARY SHEET

TITLE: Adolescent Idiopathic Scoliosis Overhang Curve

PRINCIPAL INVESTIGATOR: Polly, David W. LTC MC

DEPARTMENT: Orthopaedic Surgery and Rehabilitation

STATUS: O

SERVICE: Orthopaedic Surgery

INITIAL APPROVAL DATE: 10 April 2001

### STUDY OBJECTIVE

The main objective of this exploratory study is to help develop and define the necessary radiographic (process) and clinical (patient) outcome measures involving current surgical techniques for the treatment of single overhang adolescent idiopathic scoliosis (AIS) curves to perform a scientifically valid prospective investigation. To reflect current surgical techniques, consecutive cases of single overhang AIS curves treated surgically from 1 July 1996 to 1 April 1999 will be collected from spinal deformity centers with appropriate case volume, research capabilities, and study commitment. To achieve this goal, the pilot study will develop the infrastructure to: 1) Classify single "overhang" AIS curves reliably by different scoliosis surgeons, and 2) to ensure that participating spinal deformity centers will be able to fulfill the above requirements with an appropriate case volume to participate in a prospective investigation. A secondary objective of this exploratory study is to obtain preliminary data on currently available surgical approaches to treat these single "overhang" AIS, thoracic thoracolumbar and lumbar curve patterns, investigating the following questions: 1) Are levels truly saved using anterior versus posterior current techniques? 2) Which technique(s) provide the best correction, balance, cosmesis, and patient satisfaction? 3) Is there one technique associated with increased morbidity over others? 4) Are the cost profiles of the current techniques available and similar? 5) How does sagittal plane alignment influence the results? It is hoped that information from this secondary objective will help provide specific and detailed objectives for the future prospective investigation.

### TECHNICAL APPROACH

An exploratory study. X-ray films will be measured from the patient's immediate post-op and one-year and two-year follow-ups. Graphic illustrations of the measuring techniques will be given to each participating physician. These techniques are the standard accepted techniques as agreed upon the Scoliosis Research Society.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

To date, the software for measuring the scoliosis films has been developed and participating sites that have received their IRB approval are actively capturing the images electronically for measurement. Three spine surgeons have finished Phase 1 of the validation of the software.

Phase 2 consists of measuring the same numbered radiographs digitally on the computer and transmitting that information to PhDX for statistical significance. The end result will be to compare manual to digital for validation of the software. Because this is a retrospective review of available scoliosis films, there are no adverse events to report. Phase 2 is now completed as of December 2002. The software has been validated and the next generation software is being developed for the prospective study to be sent out to participating sites with IRB approval by May 2003.

The number of subjects enrolled to the study since last APR at WRAMC is 2 and the total enrolled to date at WRAMC is 36. The total number enrolled study-wide is 376 if multi-site study.

### CONCLUSIONS

On all but one measurement, (Sagittal T2-T5), the manual measurement technique provided a reliable and reproducible means of validating measurement methods between the surgeons. The Phase 2 statistical validations for the digital-to-digital and manual-to-digital measurement techniques are being re-evaluated due to an error from PhDX e-systems. We expect greater statistical significance for the inter- and intra-rater reliability.

## DETAIL SUMMARY SHEET

**TITLE:** A Multi-Center Study to Evaluate the Safety and Efficacy of DePuy AcroMed Titanium Surgical Mesh and Moss-Miami Spinal System Pedicle Screws

**PRINCIPAL INVESTIGATOR:** Polly, David W. LTC MC

**ASSOCIATES:** Kuklo, Timothy R. LTC MC

**DEPARTMENT:** Orthopedic Surgery and Rehabilitation

**STATUS:** O

**SERVICE:** Orthopedic Surgery

**INITIAL APPROVAL DATE:** 24 April 2001

### STUDY OBJECTIVE:

Determine the clinical success of the Titanium Surgical Mesh and MOSS-Miami Pedicle Screws in the treatment of one or two adjacent levels of degenerative disc disease in the lumbar spine. Instrumentation for this procedure is used at the levels above and or below the motion segment or segments. In addition, the clinician will be allowed to instrument at an additional level if the clinician deems it necessary. The maximum number of levels allowed to be instrumented will be four.

- Determine the rate of healing (radiographically apparent fusion) for subjects implanted with Titanium Surgical Mesh and MOSS-Miami Pedicle Screws.
- Determine the comparative success rates of the DePuy AcroMed Titanium Surgical Mesh and MOSS-Miami Pedicle Screws compared with Lumbar I/F Cage® with VSP® Spine System.
- Identify possible intra-operative complications.
- Identify possible long-term complications

### TECHNICAL APPROACH:

Preoperative Evaluation: Subjects will be asked to participate in the study following the surgeon's determination that the study criteria. The subject will be asked to sign the informed consent form following explanation and discussion of the study with the investigator. Women of childbearing age must take a blood pregnancy test before starting this study. If this test is positive, you cannot take part in this study. Once the consent form is signed the subject is enrolled in the study. The Case Report Form should be completed verifying that the investigator determined that the subject satisfied all the inclusion and exclusion criteria. (Sample Case Report Forms detailing the required data collection are provided in the Investigator Manual.) The Subject will be prepared for surgery in accordance with accepted medical practice. The appropriate history, physical examination and x-ray work will be done. The preoperative evaluation must occur within three months of the planned surgery. The preoperative evaluation is to be documented on the Demographic Case Report Form. In addition, the subject will be asked to complete the Oswestry Disability Index and the SF36 within three months prior to the surgery. The clinical coordinator will administer these research tools. The research part of the study involves the data collection from the SF-36 (a measure of health status), the Oswestry Disability Index, the Clinical Evaluation sheets and the safety and efficacy of the Titanium Surgical Mesh and MOSS-Miami Pedicle Screws versus the Lumbar I/F (Interbody Fusion) Case with the VSP Spine System using the TLIF/PLIF surgical technique. The VSP Spine System and the Lumbar I/F are outside controls use by DePuy.

Pre-operative Evaluation Data Collection: Patient demographics and history - (CRF Demographic to be completed within three months prior to surgery).

- Age
- Gender
- Height/Weight
- Smoking status
- Duration of pain (back, leg)
- Previous surgeries/treatments



Clinical Assessment:

- Pain and function status (Oswestry)
- Pain at back, leg (5 point scale)
- Work status
- Patient satisfaction questionnaire (SF36)

Radiographic Assessment:

- Anteroposterior
- Lateral
- Flexion/Extension

The pre-operative evaluation must be completed no greater than three months prior to surgery.

**Surgical Procedure:** The surgical procedure will be done on an in-patient basis as is customary for lumbar fusion surgery. The surgical approach will include PLIF and TLIF, per surgeon preference, as both are considered open posterior approaches. Post-operatively, the patient will be allowed to ambulate according to the individual surgeon's judgment. Subjects will receive standard post-operative care. Subjects should avoid bending, lifting, stooping, and twisting for the first three months. They should avoid heavy lifting for the first six months. Throughout the study, the occurrence of complications and adverse events will be identified and documented by the Study Investigator and reported to the sponsor. Based on the study results, or if deemed necessary by the clinical investigator or reviewing IRB, the sponsor will amend the study protocol, or, if warranted, terminate subject enrollment. Any additional procedures must be documented.

Intraoperative/Immediate Postoperative Assessment and Data Collection:

- Date of surgery
- Operative time
- Estimated blood loss
- Blood replacement
- Levels fused
- Device used (size and quantity)
- Complications

Surgical procedures subsequent to the original surgery will be categorized as follows:

- A revision is a procedure that adjusts or in any way modifies the original implant configuration. This may include adjusting the position of the original configuration or replacing part or all of the assembly.
- A removal is a procedure where one or more components of the original implant configuration are removed without replacement.
- A re-operation is any surgical procedure at the involved spinal level(s) that does not remove, modify, or add any components of the assembly.
- A supplemental fixation is a procedure in which additional instrumentation not under study in the protocol is implanted.
- Any implant that is removed will be returned to the Sponsor for evaluation. Retrieved implants should be stored in formalin and returned to the sponsor.

**Postoperative Evaluation:** Clinical post-operative evaluations will be performed at 3, 6, 12 and 24 months. Clinical evaluation will include pain and function, pain at donor site, pain medications, reflexes, sensory function, motor functions, and work status. Data will be collected and recorded on the follow-up CRF. All complications (device and non-device), re-operations and revisions will also be recorded at each visit on CRF Medical Event Form. At the 12 and 24-month evaluations, subjects will be asked to complete the SF-36 questionnaire. There have been no modifications to this study.

**PRIOR AND CURRENT PROGRESS:** The number of subjects enrolled to the study since last APR at WRAMC is 0 and total enrolled to date at WRAMC is 6. The total number enrolled study-wide is 112, if multi-site study. We originally had 7 enrolled, but one dropped out prior to surgery. The study sponsor informed us not to count that patient as enrolled.

**CONCLUSIONS:**

Unchanged.

## DETAIL SUMMARY SHEET

**TITLE:** Functional and Clinical Outcome Following Arthroscopically Assisted Anterior and Posterior Cruciate Ligament Reconstruction in a High-Demand Patient Population

**KEYWORDS:** Anterior/Posterior Cruciate Ligament, Surgery, Outcomes

**PRINCIPAL INVESTIGATOR:** Taylor, Kenneth F. MAJ, MC

**ASSOCIATES:** Kevin L. Kirk CPT, MC, Kevin P. Murphy LTC, MC

**DEPARTMENT:** Orthopaedic Surgery and Rehabilitation

**STATUS:** O

**SERVICE:** Orthopaedic Surgery

**INITIAL APPROVAL DATE:** 26 June 2001

### STUDY OBJECTIVE

To describe the clinical and functional outcomes of arthroscopically assisted anterior and posterior ligament reconstruction in a physically active population.

### TECHNICAL APPROACH

Retrospective chart review, clinical survey, and examination of the above patient population. No modifications in approach from initial protocol.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

To the investigator's knowledge, there have been no recent investigations of multi-ligamentously injured knees in an active population published in the literature. Findings thus far appear to demonstrate a quicker return to pre-injury activity level in patients who have undergone reconstruction with allograft ligaments compared to those who have had autograft reconstructions. This finding is also corroborated by the higher return to duty rates of the active duty patients with allograft reconstructions. Overall, the present results indicate a high patient satisfaction with the surgery as well as a large majority able to return to pre-injury function. There have been no adverse effects noted. No patient has withdrawn from the study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 16.

### CONCLUSIONS

- 1) Arthroscopically assisted ACL/PCL reconstruction allows a majority of patients to return to high levels of activity following surgery.
- 2) Allograft reconstructions allow quicker return to pre-injury activity level and had higher retention of active duty soldiers than autograft reconstruction.
- 3) Arthroscopically assisted ACL/PCL reconstruction is an excellent option for previously active patients with multiple knee ligament injury.

## DETAIL SUMMARY SHEET

TITLE: Effects of Alendronate Sodium (FOSAMAX) on Spinal Fusion in the Rabbit Model

PRINCIPAL INVESTIGATOR: Ronald A. Lehman, Jr., CPT, MC

ASSOCIATES: Timothy R. Kuklo, LTC MC; Rebecca Cockman-Thomas, LTC, VC; Jerry Cowart, DVM

DEPARTMENT: Orthopaedics and Rehabilitation

STATUS: C

SERVICE: Orthopedic Surgery

INITIAL APPROVAL DATE: 14 August 2001

### STUDY OBJECTIVE:

Alendronate sodium will not have a positive effect on bone healing by virtue of its specific inhibition of osteoclast-mediated bone resorption.

### TECHNICAL APPROACH:

Our goal is to perform bilateral intertransverse process fusion surgery using bilateral autologous iliac crest bone graft spinal fusion (as described by Boden, et. al., 1994) on skeletally mature (3-5kg) NZW rabbits. Postoperatively, we will randomly assign equal numbers to two experimental groups. Preoperative posteroanterior and lateral radiographs will be taken to help exclude specimens with underlying disease. Group 1- saline control will receive a daily postoperative dose of saline per os, while Group 2 – alendronate sodium group will receive 100ug in daily oral doses of equal volume (20-40cc) to that of the saline group. All groups will receive single daily doses by gavage of the prescribed compound for 8 weeks. After the 8-week period the animals will be humanely sacrificed and several analyses performed. At the time of sacrifice we will radiograph the lumbar spine of each rabbit. The radiographs will be viewed and the fusion mass graded in a blinded fashion as fused or not fused. Assessments will be made of the incorporation of the bone graft and that status of the fusion. This will be determined on radiographs as having a continuous trabecular pattern within the fusion mass on either side (or both sides) between the adjacent transverse processes. Incorporation of the bone graft will be graded as resorbed, minimally remodeled, moderately remodeled, or fully remodeled. Bone graft will only be placed between the transverse processes, and not between the intervening vertebral bodies. After radiography, the lumbar spine and fusion mass will be excised and grossly inspected. Gross size of each fusion will be noted. At this time manual palpation of the fusion mass will be performed. Two trained individuals, blinded to the treatment group, will evaluate the fusion mass as solid (no movement) or not solid (movement present) at the level of the joint fused. The location of the motion will be noted when present. Only levels that have had graft incorporation and no motion in the fusion mass will be defined as fused. A veterinary pathologist will perform histological analysis. The quality of the fusion will be graded at the level by assigning a histologic score from zero to seven as described by Emery et al. The area of focus will be at the superior and inferior transverse process and bone graft incorporation sites. The superior and inferior sites will be sampled, and their scores averaged. Then, the right and left scores will be averaged and a mean score assigned to each rabbit. The lumbar spine at the level of the arthrodesis will be prepared for histologic analysis.

### PRIOR AND CURRENT PROGRESS

The study is completed. All research data has been accumulated, analyzed and the manuscript written and pending acceptance in The Spine Journal.

### CONCLUSIONS

Research Complete.

Have not used the travel money - \$1000.00.

## DETAIL SUMMARY SHEET

TITLE: Dead Regions in the Cochlea and Their Influence on Speech Processing

KEYWORDS: cochlear processing, inner hair cells, hearing loss, amplification

PRINCIPAL INVESTIGATOR: Summers, Van Ph.D. DAC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: O

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 7 November 2000

### STUDY OBJECTIVE

To test for regions of dead inner hair cells in cochleas of listeners with high-frequency hearing loss. To examine the influence of high-frequency amplification on speech recognition performance for hearing-impaired listeners with and without dead inner-hair-cell regions.

### TECHNICAL APPROACH

The study involves three psychoacoustic tasks (masked thresholds in threshold equalizing noise, psychophysical tuning curves, and frequency modulation detection) aimed at identifying listeners with regions of dead inner hair cells or nonfunctioning neural channels in the cochlea. The second portion of study involves tests of speech recognition under various amplification conditions to determine the benefit of amplifying frequencies associated with these "dead regions".

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Data collection is completed and a manuscript describing the results has been submitted to Ear and Hearing. The TEN and PTC results were in agreement in identifying the presence or absence of dead regions in only 10 or 18 ears (~56% agreement rate). The speech recognition results did not provide clear evidence that the presence or absence of dead inner hair cell regions will influence what amplification strategy is most likely to benefit a given hearing-impaired listener.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 17. None of the subjects have withdrawn from the study. There have been no adverse reactions from subjects. There is no benefit to the subjects.

### CONCLUSIONS

The listeners tested in this study have near-normal low-frequency hearing and steeply sloping high-frequency hearing loss. The TEN and PTC tasks frequently produced conflicting results concerning whether dead inner hair cell regions were present for a given listener. In the speech testing, listeners generally showed little benefit from either the broadband amplification generally provided by hearing aids or lowpass amplification aimed at avoiding amplification of frequencies associated with dead regions. Diagnosis of the presence of dead regions based on the TEN and PTC results did not appear to influence this general pattern.

## DETAIL SUMMARY SHEET

TITLE: Spread of Masking by Harmonic Complexes in Normal Hearing and Hearing Impaired Listeners

KEYWORDS: Masking, Schroeder-phase, harmonics

PRINCIPAL INVESTIGATOR: Leek, Marjorie R. Ph.D, DAC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Army Audiology & Speech Center

STATUS: C  
INITIAL APPROVAL DATE: 12 June 2001

### STUDY OBJECTIVE

To determine the influence of acoustic waveform shape on the upward spread of masking from low frequencies to high frequencies within harmonic complexes. Excessive acoustic interference across frequency for waveforms shaped like vowel sounds might be involved in some of the difficulties experienced by hearing-impaired people while listening to speech sounds in noisy environments.

### TECHNICAL APPROACH

Masking by harmonic complexes will be measured in a two-alternative forced choice procedure with signal frequencies ranging from 1000 to 4000 Hz. Signal frequencies at and below 2000 Hz fall within the passband of the masker, while higher frequencies measure masking outside the masker passband. Masking will be measured at three masker levels, and for maskers constructed with component phases in positive and negative Schroeder phases. Masking will also be measured for a Gaussian noise with the same frequency passband as the harmonic complexes.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Data collection is completed on this study. No new subjects were enrolled during the last year. One subject chose to withdraw from the study without completing it due to difficulty finding time to attend the experimental sessions. There have been no adverse reactions. There is no direct benefit to the subjects from participating in the study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 12.

### CONCLUSIONS

Upward spread of masking by harmonic complexes increased with increasing stimulus intensity. The positive Schroeder-phase masker was less effective at masking on-frequency signals than negative Schroeder-phase masker. However, the reverse was true for signal frequencies signals higher than the masker band. More upward spread of masking was found for hearing-impaired subjects, but the reversals in masking effectiveness due to masker phase were also observed in those listeners. These findings may reflect a change in phase in the low-frequency skirts of the auditory filters underlying masking effects, and an interaction between the masker waveforms and neural tuning curves.

## DETAIL SUMMARY SHEET

TITLE: SWOG Selenium and Vitamin E Cancer Prevention Trial (SELECT), Phase III Study

KEYWORDS: Selenium, Vitamin E, Cancer prevention, Prostate

PRINCIPAL INVESTIGATOR: Dean, Robert LTC MC

ASSOCIATES: Judd Moul COL MC; David McLeod COL MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: Urology

INITIAL APPROVAL DATE: 20 February 2001

### STUDY OBJECTIVE

Primary objective is to assess the effect of selenium and vitamin E alone and in combination on the clinical incidence of prostate cancer. Secondary objectives are: to assess the effect of these two drugs alone and in combination on the incidence of other cancers including lung, colorectal, and all other cancers combined; to assess the effect of the study drugs alone and in combination of prostate cancer free survival, lung cancer free survival, colorectal cancer free survival, cancer free survival, overall survival, and serious cardiovascular events. Quality of life, molecular epidemiology, pathological biomarkers, and diet supplement, nutrient intake, and plasma nutrients will also be assessed.

### TECHNICAL APPROACH

A total of 150 to 400 men who are in good health will be enrolled at WRAMC over a period of five years or until the enrollment goal is reached. The study will last a total of seven to twelve years for each man, depending upon the date of enrollment. The digital rectal exam (DRE) must be normal, and the prostate specific antigen (PSA) must be at or below 4 ng/ml. African American men must be at least fifty years old; all other races fifty-five years old. The men are ineligible if they have any previous history of hemorrhagic stroke or have had a malignancy other than basal or squamous cell carcinoma within the last five years, or are on coumadin for any reason. There will be two visits required per year. The annual visit consists of: DRE and blood draw for PSA, dispensing of a six-month supply of study drugs, and a general health assessment. The second visit at six months after enrollment will be for general health assessment and medication dispensing. The men enrolled have the choice of participating in several sub-studies that involve the collection of toenails, blood, and prostate tissue (only if biopsy is indicated by a rise in PSA or abnormal DRE) for current and future research of prostate cancer.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been 88 men enrolled since the last APR, for a total of 88. There have been no serious adverse events here at WRAMC or at any other of the 400+ sites. No patients have withdrawn from the study at WRAMC; however, one is moving out of the area and transferring to another site in January 2003.

There has been no literature published to date and no study findings. Sponsor amendment #1 dated 14 February 2002 was approved with revisions on 28 May 2002 (consent change). Request for change of PI was made 31 July 2002 and included a consent change (for clarification). Approval is pending.

PREADVISE sub-study protocol was submitted 24 April 2002. Requested revisions have been made and resubmitted, and approval is pending.

The number of subjects enrolled to the study since last APR at WRAMC is 88 and the total enrolled to date at WRAMC is 88. The total number enrolled study-wide is >16,000. Study-wide goal is 32,000+. Enrollment is ahead of schedule.

### CONCLUSIONS

There have been no conclusions to date.

## DETAIL SUMMARY SHEET

**TITLE:** A Pilot Study to Evaluate the Safety and Feasibility of Thermal Ablation with Thermo Rods for Residual Prostate Cancer Following External Beam Radiation Therapy.

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** McLeod, David COL, MC  
**ASSOCIATES:**

**DEPARTMENT:** Surgery  
**SERVICE:** Urology

**STATUS:** O  
**INITIAL APPROVAL DATE:** 20 March 2001

### STUDY OBJECTIVE

The primary objective is to evaluate the safety of a course of thermal ablation treatment with Thermo Rods to treat residual prostate cancer following external beam radiation therapy. The secondary objective is to obtain preliminary data, as a follow-up to this study, regarding the effect of thermal ablation with Thermo Rods on PSA levels over time.

### TECHNICAL APPROACH

This is an open, multi-center, non-randomized, uncontrolled pilot study to evaluate the safety and feasibility of Thermal Ablation with Thermo Rods for residual prostate cancer following external beam radiation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This protocol received final approval on 20 March 2001. Sponsor-initiated changes to the protocol were submitted to the WRAMC IRB and approved on 12 March 2002. The number of subjects enrolled to the study since last APR at WRAMC is 4 and the total enrolled to date at WRAMC is 4. The total enrolled study-wide is 18. No patients have withdrawn from the study. We have received no new adverse reports from the sponsor. All serious and unexpected adverse events from WRAMC have been reported. Enrollment in the study has been suspended by the sponsor due to a setback in funding for Thermo Rod treatment.

### CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: AMS002.2 - Evaluation of the Safety and Tolerability of Transurethral Dehydrated Alcohol Injection for the Treatment of Benign Prostatic Hyperplasia

KEYWORDS:

PRINCIPAL INVESTIGATOR: COL David McLeod MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: C  
INITIAL APPROVAL DATE: 15 May 2001

### STUDY OBJECTIVE

The primary objectives of this study are to monitor the occurrence of side effects and complications associated with transurethral injection of dehydrated alcohol into the prostate and establish a dose range that provides improvement in symptoms with minimal side effects.

The secondary objectives are to evaluate the improvement in lower urinary tract symptoms (LUTS) in men with Benign Prostatic Hyperplasia (BPH) following transurethral intraprostatic injection of dehydrated alcohol and to assess the impact of treatment on patient sexual function and quality of life.

### TECHNICAL APPROACH

This is a phase I-II study to evaluate the safety and tolerability of transurethral dehydrated alcohol injection for the treatment of benign prostatic hyperplasia.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This protocol received final approval on 15 May 2001. As a result of a sponsor-reported serious adverse event, which occurred at another site, and discussion with the FDA on 10 August 2001, this protocol was placed on clinical hold and enrollment was suspended. The adverse event has been reported to the WRAMC IRB. On 4 March 2002, the sponsor announced that the FDA released this study from clinical hold. On 22 March 2002, we received the revised protocol incorporating the FDA requirements and submitted the addendum to DCI for approval. The addendum was approved on 27 August 2002.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to-date at WRAMC is 0. The total enrolled study-wide is 80 if multi-site study. We have received no new adverse events reports from the sponsor.

### CONCLUSIONS

None to date. No patients have been enrolled in this study. The sponsor has closed on randomized group enrollment. Based on these factors, the PI has decided to close this protocol.



## DETAIL SUMMARY SHEET

TITLE: An Exploratory Comparison Between Lemonade and Potassium Citrate - The Impact on Urine pH and 24 Hour Urine Parameters

KEYWORDS:

PRINCIPAL INVESTIGATOR: MAJ Kevin Gancarczyk MC

ASSOCIATES: LTC Noah Schenkman MC

DEPARTMENT: Surgery

SERVICE: Urology Service

STATUS: O

INITIAL APPROVAL DATE: 26 June 2001

### STUDY OBJECTIVE

To explore the effects of lemonade on 24-hour urinalysis parameters, in patients with a history of nephrolithiasis, compared to the standard urinary alkalinizing agent, potassium citrate.

### TECHNICAL APPROACH

This is a self-controlled, pilot study to examine the changes in a 24 hour urine specimen in a small collection of subjects, who are treated sequentially on (1) Dietary treatment, (2) Lemonade, and (3) Potassium citrate tablets.

The subjects and the investigators will be not be blinded. Subjects will be instructed to maintain a low sodium, low protein diet that is helpful in preventing stone formation for the duration of the study. Appropriate female subjects will have a pregnancy test done at the beginning of the study, although none of the treatments have any known teratogenic effects.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No new recent literature. One patient withdrew from study due to gastrointestinal side effects of the potassium citrate.

The number of subjects enrolled to the study since last APR at WRAMC is 15 and the total enrolled to date at WRAMC is 21.

### CONCLUSIONS

Several patients are in various stages of completing the study and final analysis is pending. We are currently not actively enrolling patients as we have met our goal of 20. However, if some do not complete the study recruitment will resume.

## DETAIL SUMMARY SHEET

TITLE: Outcome Comparison of Radical Prostatectomy Pathologic Specimens

PRINCIPAL INVESTIGATOR: Moul, Judd COL MC

ASSOCIATES:

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: C

INITIAL APPROVAL DATE: 1 May 2001

MASTER PROTOCOL APPROVAL DATE: 26 May 1998

### STUDY OBJECTIVE

It is hypothesized that the step sectioning of whole mounted prostate specimens would enhance the ability to discover violation of surgical margins and extra-capsular extension, resulting in decreased recurrence (biochemical and clinical) in patients with negative margins, and greater identification of patients with positive margins.

### TECHNICAL APPROACH

We have reviewed the articles related to outcomes of radical prostatectomy and prognostic factors affecting the outcomes by using PubMed and manual literature search to get the hypothesis stated above. A SQL script will be written to query the CPDR prostate cancer database (WU #2857-98) for data from the data fields listed below. The data set will be divided into two groups based on the processing methods of radical prostatectomy specimens: "Whole mount" group in which the specimen were processed with whole-mounted and step sectioning (2.25 mm thick) technique, and "Non-whole mount" group in which the specimens were processed with traditional hand slicing (2-5 mm thick) and partial sampling method. Comparison of pathological findings of the radical prostatectomy specimens between the whole-mounted group and non-whole mount group will be performed, and the relationship between the pathological findings and disease-free survival will be analyzed.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found.

This study was approved as closed by the WRAMC HUC on 14 May 2002. The protocol was then approved as re-opened 25 October 2002. This allowed for the addition of National Naval Medical Center as a site for the study with LCDR Timothy F. Donahue as a Collaborator.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 249. The total number enrolled study-wide is 931 if multi-site study.

### CONCLUSIONS

Close-step sectioning and whole mounting of radical prostatectomy specimens provides a more accurate assessment of pathologic stage. For standard processed radical prostatectomy specimens, there is a higher false staging such that many men thought to have "organ confined" disease actually have subtle extraprostatic extension that is only detected by the close-sectioning/whole mount technique.

## DETAIL SUMMARY SHEET

TITLE: Study of CPDR Multicenter Database to Develop Nomograms on % of Positive Biopsy Cores, Gleason Sum, and Pre-Biopsy PSA to Predict Pathologic Stage in Radical Prostatectomy Patients

PRINCIPAL INVESTIGATOR: Moul, Judd COL MC

ASSOCIATES: Gancarczyk, Kevin J MAJ MC

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: O

INITIAL APPROVAL DATE: 5 June 2001

MASTER PROTOCOL APPROVAL DATE: 26 May 1998

### STUDY OBJECTIVE

The goal of this study is to develop predictive nomograms based on % of core biopsies positive for prostate cancer, highest biopsy Gleason sum, and pre-treatment (or pre-biopsy PSA) to predict final pathologic stage variables in men who have undergone radical prostatectomy and whose data has been maintained in the Center for Prostate Disease Research (CPDR) multicenter database (WU#2857-98). Secondary goals will be to recreate CPDR nomograms identical to the methodology of Partin et al. using their three prognostic factors and to determine how well the Partin et al. nomograms predicted our CPDR cases.

### TECHNICAL APPROACH

The clinical and pathological data of all men entered into the Center for Prostate Disease Research's (CPDR) database, which is a Department of Defense Multi-center Tri-service Longitudinal National Database that had diagnosis by transrectal ultrasound and biopsy (TRUS/BX) and undergone radical prostatectomy as primary therapy for prostate cancer between January 1990 and January 2001 will be reviewed. Only those men that have complete information in regards to clinical stage, race, age, pre-treatment PSA, TRUS/BX data and pathologic stage will be analyzed. Required TRUS/BX data include total number of cores taken, total number of cores positive for prostate cancer and highest Gleason score. The study is limited to men that had between 6-12 cores taken and defined the percentage of biopsy cores positive as the total number of cores positive for prostate cancer divided by the total number of cores taken. All of the radical specimens were staged according to the 1992 TMN classification and only those with pathology Gleason Sum available were used. Any patient that had neoadjuvant hormonal therapy or are missing any of the aforementioned data of interest will be excluded.

Once the patients are identified, a bivariate analysis will be performed using chi square method for PSA, clinical stage, highest biopsy Gleason Sum, race, age, and percentage of biopsy cores positive for prostate cancer to determine the most significant predictors of pathologic outcome. The main objective of this study is to produce a clinically useful probability nomogram. In order to accomplish this, we have to determine the pathological stage stratification of the percent of biopsy cores positive. Biopsy cores are taken ranging from 6-12 to encompass the multiple biopsy schemes that are currently in practice. Nine subgroups will be initially formed: < 20%,  $\geq 20$  to < 30,  $\geq 30$  to < 40,  $\geq 40$  to < 50,  $\geq 50$  to < 60,  $\geq 60$  to < 70,  $\geq 70$  to < 80,  $\geq 80$  to < 90,  $\geq 90$  to 100 (16-20). Next, the four possible pathologic outcomes: organ confined (OC), capsule positive (Cap +), seminal vesicle positive (SV +) and node positive (N+) will be applied to these groups. Then, based on similar pathologic outcomes, the final subgroups will be identified. Next, the significant predictors will be entered into a stepwise logistic regression model to determine their independent predictive significance. Once the three most significant independent predictors of pathology at the time of radical prostatectomy with their subgroups are identified, a probability nomogram will be created with each patient having one pathologic outcome and a confidence level greater than 95%.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found.

Work Unit # 01-2857-98b [*Continued*]

The study included 1,527 patients and found that PSA level, biopsy worst Gleason Sum, clinical stage, and percent of biopsy cores containing cancer were all independent predictors of pathologic stage after radical prostatectomy. Nomogram tables were constructed using these factors to predict pathologic stage.

The number of subjects enrolled to the study since last APR at WRAMC is N/A and the total enrolled to date at WRAMC is 1,527.

CONCLUSIONS

The percent of biopsy cores containing prostate cancer was a clinically useful staging factor in surgically managed men with clinically localized prostate cancer.

## DETAIL SUMMARY SHEET

TITLE: Development of Internet-Accessible Prediction Models for Prostate Cancer Diagnosis, Treatment and Follow-up

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: O  
INITIAL APPROVAL DATE: 7 August 2001  
MASTER PROTOCOL APPROVAL DATE: 26 May 1998

### STUDY OBJECTIVE

- (1) Analyze the CPDR database by integrating the most powerful prognostic variables with the following regression models: logistics regression, Cox proportional regression, and artificial neural networks (ANN).
- (2) Build clinical models predicting probability of prostate cancer in the diagnosis phase, optimal primary treatment in the treatment phase, and the optimal recurrence treatment in the follow-up phase.
- (3) Implement these models into software and post it on the web accessible by patients and physicians as tools for public education, patient self-testing, and physicians decision making reference.

### TECHNICAL APPROACH

A data warehouse will be designed, and web applications to support the prediction models will be developed. Unix operating system, Oracle servers, and SAS will be used to support the web applications and data mining.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search has been performed and there are no new findings to report.

The number of subjects enrolled to the study since last APR at WRAMC is 425 and the total enrolled to date at WRAMC is 5291. The total number enrolled study-wide is 2520, if multi-site study.

### CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: Characterization of Novel Prostate Specific Gene, PCGEM1

KEYWORDS: tissue, prostate, cancer

PRINCIPAL INVESTIGATOR: Moul, Judd COL MC

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: O

INITIAL APPROVAL DATE: 20 February 2001

MASTER PROTOCOL APPROVAL DATE: 21 July 1998

### STUDY OBJECTIVE

Characterization of PCGEM1 Structure and Function

Mechanisms of Regulation of PCGEM1 Expression

Analysis of PCGEM1 Expression in Prostate Cancer

### TECHNICAL APPROACH

1. Characterization of PCGEM1 Structure and Function: A comprehensive analysis of PCGEM1 cDNA clones has revealed that PCGEM1 represents a novel cDNA sequence, which may belong to the emerging group of functional non-coding mRNAs. PCGEM1 cDNA as well as the native PCGEM1 mRNA will be analyzed to determine if PCGEM1 functions as a non-coding RNA or one of the short ORFs of the PCGEM1 cDNA encode PCGEM1 protein. PCGEM1 mRNA will be analyzed for its subcellular localization e.g. nuclear localization of PCGEM1 mRNA or absence of PCGEM1 mRNA in polyribosomes will further support its non-coding nature. Anti-peptide antibodies will be raised against PCGEM1 ORFs to detect PCGEM1 encoded protein, if any. The short ORFs derived from the PCGEM1 cDNA will be expressed in NIH3T3 cells as observed with the full length PCGEM1 cDNA. Cell growth regulating functions of the PCGEM1 will be characterized by over expression of PCGEM1 in NIH3T3 cells or immortalized normal prostate epithelial cells and by inhibiting the expression of PCGEM1 sequence LNCaP prostate cancer cells. Deletion mutagenesis will define the regions in PCGEM1 sequence critical for PCGEM1 biologic functions. The cDNA sequence of PCGEM1 homologs from non-human species will determine conserved regions of PCGEM1.

2. Mechanisms of Regulation of PCGEM1 Expression: The prostate tissue specificity and androgen regulation of PCGEM1 suggests for normal functions of PCGEM1 in development and/or maintenance of the prostate gland. Genomic clones of PCGEM1 will be characterized by DNA sequencing. The PCGEM1 promoter sequence will be identified and characterized by DNA sequencing. The PCGEM1 promoter sequence will be identified and characterized by transfecting PCGEM1 reporter-reporter constructs in LNCaP cells treated with or without androgens. Once the PCGEM1 promoter is identified, it will be analyzed for the sequence elements for the presence of androgen response elements (ARE). Deletion mutagenesis of the promoter sequence followed by reporter gene assays will be performed to define the sequences that confer prostate tissue specificity or androgen regulation. Using in situ hybridization assays, the cell type specificity of the PCGEM1 expression will be established in frozen OCT embedded and paraffin embedded tissue sections of the normal and tumor regions of the human prostate.

3. Analysis of PCGEM1 Expression in Prostate Cancer: Preliminary analysis of paired normal and tumor specimens revealed PCGEM1 over expression in tumor specimens of about half of CaP patients. Role of PCGEM1 expression in prostate cancer progression will be evaluated in CWR22 xenograft model derived tumors representing androgen sensitive and androgen refractory tumors. PCGEM1 expression will also be analyzed in matched normal and tumor tissue of 100 prostate cancer patients using laser capture micro dissection (LCM) and quantitative RT-PCR. Analysis of PCGEM1 expression by in situ RNA hybridization in representative specimens will complement the RT-PCR assays. We will examine whether PCGEM1 over expression is associated with specific pathologic stage, cancer recurrence after radical prostatectomy, and the clinical stage of the disease.

To address the PCGEM1 expression in the context of multifocal CaP, PCGEM1 expression will be analyzed in the sections of the whole-mounted prostate from cancer patients.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search has been performed and there are no new articles to report. There are no AEs to report.

This is a summary of Specific Aim 2, related to use of human specimens for evaluation of *PCGEM1* expression in CaP. The goal of this specific aim of the grant proposal is to assess if *PCGEM1* expression levels could serve as a novel biomarker for CaP risk. Quantitative *PCGEM1* expression analysis by real time RT-PCR assays in LCM derived paired normal and tumor cells from 90 CaP patients revealed cancer cell specific overexpression in about half of CaP patients. This study was done through WRAMC approved protocol WU-2871-98. A significant differential upregulation of *PCGEM1* in the CaP cells of African American men was observed. In addition, an association of *PCGEM1* overexpression in normal cells of CaP patients with family history was also detected. These are intriguing findings, as two well-defined high-risk groups for CaP are African American men and men with family history of CaP. We will enhance the *PCGEM1* analysis to validate these observations. We will continue and expand the generation of the RNA bank from normal and cancer cells, captured by LCM from OCT embedded frozen prostate tissue specimens of radical prostatectomy patients. RNA will be isolated from the LCM cells, quantitated, tested for quality and aliquoted. A bank of paired normal and tumor cell RNA stocks is currently established from over 100 patients. The LCM RNA bank will be expanded to additional 250 patients that will provide additional 75 African Americans Cap patients and 50 patients with family history of CaP based on the estimates of these groups of patients from our current study. This data from patient cohort along with the existing data will be able to clearly establish the statistical significance of *PCGEM1* over expression in African American CaP patients and familial CaP patients. RNA from paired normal and tumor cells of each patient will be screened by real time quantitative RT-PCR (TaqMan) for *PCGEM1* expression. Serum PSA levels are generally higher in African American men in comparison to Caucasian American men. Since both *PCGEM1* and PSA genes are up-regulated by male hormones, a possible link of *PCGEM1* expression modulation to male hormone pathway will be tested by correlating *PCGEM1* expression with expression of androgen receptor (AR), and androgen regulated genes: PSA and *NKX3.1*. The LCM-RNAs will be screened by real time quantitative RT-PCR (TaqMan) for the expression of these three genes the same fashion it is already done with *PCGEM1*. Due to the very heterogeneous nature of prostate cancers within individual patients, and intratumoral heterogeneity of CaP, it is a challenge to find molecular alterations that are uniformly associated within the cells of tumor tissues. Our preliminary results with *PCGEM1 in situ* hybridization shows focal staining in most biopsy sections. In a representative set of 100 patients, *PCGEM1* expression analysis will be performed by quantitative RT-PCR of LCM RNAs, and by *in situ* hybridization analysis of the whole-mounted prostate specimen sections. A non-radioactive *in situ* staining protocol is being developed in our laboratory using *PCGEM1* overexpressor cell lines, as well as tissue sections with known high or low *PCGEM1* expression from our RT-PCR assays. The protocol will be optimized for whole mount sections with the help of our collaborator on pathology and tissue related technology. Whole mount sections from at least 100 patients will be analyzed with special emphasis on high-risk population. Dr. Moul and Dr. Sesterhenn will support the PI and Co-PI with the specimen selection and clinicopathologic evaluations. Dr. Sun will provide the patient database support. Mr. Connelly, the biostatistician, will provide support for the statistical evaluations of the data.

The number of subjects enrolled to the study since last APR at WRAMC is 72 and the total enrolled to date at WRAMC is 150.

#### CONCLUSIONS:

None at this time.

## DETAIL SUMMARY SHEET

TITLE: The Use of Transformed Prostate Cell Lines CPDR7, CPDR8, CPDR9, to Evaluate the Capacity of T Lymphocytes to Recognized Prostate-Derived Antigens

## KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: C  
INITIAL APPROVAL DATE: 10 April 2001  
MASTER PROTOCOL APPROVAL DATE: 21 July 1998

STUDY OBJECTIVE

The CPDR7, CPDR8 and CPDR9 cell lines will be used as target cells in cytotoxicity *in vitro* assays to determine whether peptide-specific CTL can recognize naturally processed antigen.

TECHNICAL APPROACH

CPDR7, CPDR8, and CPDR9 immortalized prostate cancer cell lines will be used as targets in the cytotoxicity assays in addition to T2 cells. This will specifically help to demonstrate that naturally processed antigens can be lysed by CTL to peptides.

*Day 0 Generation of Dendritic Cells (DC):* Monocytes are purified by plating  $10 \times 10^6$  PBMC in 3 ml of complete medium (RPMI-1640 plus 5% AB hum serum, non-essential AA sodium pyruvate, L-glutamine and gentamycin) in each well of a 6-well plate. After two hours at 37° C, the non-adherent cells are removed by gently shaking the plates and aspirating the supernatants with a Pasteur pipette and vacuum. The wells are washed for a total of three times with medium (3 ml) to remove most of the non-adherent and loosely adherent cells. Check the plates in the inverted microscope and if contaminating T cells are still present, remove them by gently flushing medium onto the bottom of the wells with a transfer pipette and removing one more time the supernatants. Add 3 ml of complete medium to each well containing 50 ng/ml of GM-CSF and 1,000 U/ml of IL-4. These DC will be ready to use for CTL induction cultures after 6-7 days. IF the cell cultures become too yellow, remove ½ of medium and feed with fresh medium containing cytokines. On day 6, DC can be induced to mature by adding fresh medium containing poly I:C (Sigma) to a final concentration of 20 µg/ml.

*Day 7 (part A) Induction of CTL with DC and peptide:* The DC are harvested and washed 1X with PBS-HAS (human serum albumin) and re-suspended in PBS with 1% HSA. The DC are counted and pulsed with 40 µg/ml of synthetic peptides corresponding to prostate antigens (PSA, PSMA, etc...) at a cell concentration of  $1\sim 2 \times 10^6$ /ml in PBS-HSA in the presence of 3 µg/ml  $\beta_2$  microglobulin for four hours at 20°C (room temperature) with constant mixing in rocking platform. While the DC are being pulsed, CD8<sup>+</sup>T-cells are purified with Miltenyi immunomagnetic beads by positive selection as described above for CD14<sup>+</sup>cells and will be used as responders. CD8-depleted cells can be re-frozen for use as monocytes for re-stimulation with antigen (day 14). Typically, to obtain enough cells for one 48-well plate culture, 200 to  $250 \times 10^6$  PBMC are processed to obtain  $24 \times 10^6$  CD8<sup>+</sup>cells. Re-suspend the CD8 positive cells after washing them at  $2 \times 10^6$  cells/ml and keep at 4°C until further use. After the 4 hr peptide pulsing incubation, the DC are irradiated (4,200 rads), washed 1 time with RPMI-HS medium (RPMI + 5% human AB serum), and diluted at  $1 \times 10^5$  cells/ml.

*Day 7 (part B) Setting up T-cell priming cultures:* 0.25 ml cytokine-generated DC (@  $1 \times 10^5$  cells/ml) are co-cultured with 0.25 ml of CD8 T-cells (@  $20 \times 10^5$  cells/ml) in each well of a 48-well plate in RPMI-HS and in the presence of 10 ng/ml of rIL-7.



Day 8 Add rIL-10 to a final concentration of 10 ng/ml.

Day 14 Restimulate the induction cultures with peptide pulsed adherent cells in individual wells of the 48-well plate: Plate  $2 \times 10^6$  PBMC (washed with DNase and irradiated ~4,200 rads) in 0.5 ml of the complete medium per well. Incubate for 2 hours at 37°C to allow monocytes to adhere to bottom of plates. Wash off non-adherent cells by gently flushing the cells with PBS 2% FCS and pulse adherent cells with 10 µg/ml of peptide in the presence of 3 µg/ml  $\beta_2$  microglobulin (in 0.25 ml of PBS-FCS per well) for 2 hours at room temperature in rocking platform. The peptide solution from each well is aspirated. One-half of the media is aspirated from the CD8+ cells and fresh media. The cells are re-suspended individually and transferred to the wells containing the “dry” peptide-pulsed adherent cells.

Day 15 Add 100 µl of medium containing rIL-10 and rIL-4 (1:100) so final concentration of cytokines is 10 ng/ml and 2000 U/ml.

Day 16 or 17 Add 100 µl fresh medium containing rIL-2/ml (final of 50 IU) to each well.

Day 21 Re-stimulate the entire cultures again. Repeat procedures from day 7 to 17.

Day 28-29 Perform either a cytotoxicity (5 hr Cr<sup>51</sup> release) assay or ELISA for individual wells using a single E/T ratio (use 75% of the cells from each well, and do not count the effectors). Targets used are: T2, T2-pulsed with peptide (10 µg/ml the night before). In addition, the CTL will be tested for activity against the CPDR7, CPDR8 and CPDR9 cell lines to demonstrate that these cells can recognize naturally processed antigens. CPDR 7, CPDR 8 and CPDR 9 cell lines will be used as targets in cytotoxicity assays by labeling with 51Cr.

\*\*To continue growing positive wells, the cultures must be re-stimulated with peptide and APC every 7 days as described above or expanded by REM.

NOTE: Peptides were provided diluted in 100% DMSO plus 0.1%TFA at 20 mg/ml. A total of 5 mg are in each vial - sufficient for several experiments. Dilute in medium for pulsing APC or targets only the amount required. Peptide stocks can be stored at -20°C and frozen and thawed several times (up to 10) without problem.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are no AEs to report. Due to the inability to successfully grow the cultures, this protocol is being closed.

Reporting a count of subjects enrolled on this protocol is not applicable, as this protocol uses three cell lines, CPDR7, CPDR8 and CPDR9 that were developed under the master protocol WU# 2871-98 “Creation of a Tissue Library for the Molecular Biologic Study of Patients with Prostate Cancer”.

The number of subjects enrolled to the study since last APR at WRAMC is N/A and the total enrolled to date at WRAMC is N/A. The total number enrolled study-wide is N/A, if multi-site study.

#### CONCLUSIONS

None.

## DETAIL SUMMARY SHEET

TITLE: Characterization of Prostate Specific G-Protein Coupled Receptor (PSGR) in Prostate Cancer

PRINCIPAL INVESTIGATOR: Moul, Judd COL MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: Urology

INITIAL APPROVAL DATE: 7 August 2001

MASTER PROTOCOL APPROVAL DATE: 21 July 1998

### STUDY OBJECTIVE

PSGR will be analyzed for its biologic and biochemical functions and expression. Tumor tissues, well characterized for pathology and clinical information, will be used to evaluate the prognostic utility of PSGR overexpression in prostate tumor development and/or progression.

### TECHNICAL APPROACH

#### Year 1

Task 1: Prepare polyclonal antibodies against PSGR synthetic peptides.

Task 2: Bacterial expression of full length and partial PSGR protein and generation of antibodies against bacterially expressed/purified PSGR antigens.

Task 3: Evaluate PSGR expression vectors (AdPSGR and plasmid-expression vectors) for analysis of biologic and biochemical functions in prostatic epithelial cells.

Task 4: Characterize anti-PSGR antibodies by immunoprecipitations, Western blot and immunofluorescence/immunocytochemistry for detection of the PSGR protein in PSGR transfectants and bacterially expressed PSGR protein.

Task 5: Cell biologic characterization of prostatic epithelial cells harboring expression vectors of PSGR. Evaluation of PSGR transfectants in cell cycle and apoptosis assays. Analysis of the PSGR transfectants in colony forming, soft agar and cell proliferation assays.

Task 6: Screening and characterization for PSGR expression in prostate cancer cell lines.

Task 7: Prepare RNA from laser micro dissected matched normal and tumor specimens of 50 prostate cancer patient and analyze for PSGR expression by quantitative RT-PCR using TaqMan chemistry and ABI 7700 system (50 samples per year).

#### Year 2

Task 1: Characterization of the genomic clone of PSGR and sequence analysis of putative promoter sequence.

Task 2: Analyze promoter sequence of PSGR using luciferase reporter gene assays and transient transfections of prostate cancer cells and CoS cells.

Task 3: Follow up on the cell biologic characterization of PSGR transfectants.

Task 4: Study the membrane localization of the PSGR protein.

Task 5: Analysis of biochemical properties of PSGR: dissection of the signal transduction pathways.

Task 6: Optimize and analyze the analysis of PSGR protein by immunohistochemistry in prostate tissues, determine cell type specificity, and get the tissue array ready. If antibodies do not work, this line of experiment will be discontinued.

Task 7: Prepare RNA from laser micro dissected matched normal and tumor specimens of 50 prostate cancer patients and analyze for PSGR expression by quantitative RY-PCR using TaqMan chemistry and ABI 7700 system (50 samples per year).

Year 3

Task 1: Analysis of PSGR expression in prostate tissues by *in situ* RNA hybridization and immunohistochemistry.

Task 2: Analyze tissue microarray of 425 prostate cancer patients for PSGR protein expression.

Task 3: Prepare RNA from laser micro dissected matched normal and tumor specimens of 50 prostate cancer patient and analyze for PSGR expression by quantitative RT-PCR using TaqMan chemistry and ABI 7700 system (50 samples per year).

Task 4: Complete clinico-pathologic correlation and statistical analysis of the PSGR expression (both by quantitative RT-PCR and immunohistochemistry) in specimens from prostate cancer patients.

Task 5: Follow up on the biochemical characterization of PSGR functions.

Task 6: Utilizing deletion mutagenesis approach, characterize the cell/tissue specificity conferring cis-acting sequences in the promoter region and study the enhancer elements, if any.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

1. Function analyses. PSGR is a G protein-coupled receptor and is overexpressed in prostate cancer. We predicted that PSGR might be involved in signal transduction and cell proliferation. To assess the effect of PSGR on cell growth, we first generated several expression vectors, such as PSGR adenovirus expression vector, PSGR-V5 plasmid, PSGR-flag plasmid, PSGR-GFP plasmid and PSGR mutant plasmid. All the vectors were sequenced to verify the correct sequence of PSGR. These vectors are currently been testing in cell proliferation assays (colony forming, cell cycle and apoptosis).
2. Expression analysis. As a highly prostate specific gene, PSGR may be a potential diagnosis and/or prognosis marker for prostate cancer (CaP). Careful analysis of expression profile of PSGR in CaP will provide further information regarding the function of this gene and the role of this gene in CaP development. Matched normal and tumor prostate tissues from 110 CaP patients were processed for laser capture microdissection (LCM) to harvest prostate epithelial cells. Total RNAs from these LCM derived cells were conducted quantitative RT-PCR using 7700 sequence detection system. The result revealed that 74 out of 110 CaP patients (67.3%) showed overexpression of PSGR. The clinico-pathologic correlation analyses are ongoing.
3. Antibody generation. Bacterial expression vector encoding PSGR protein was generated. The protein produced by the bacteria carrying the expression vector was purified and was sent to Biosynthesis for anti-PSGR antibody generation. We will receive the first bleeds by the end of November.

The number of subjects enrolled to the study since last APR at WRAMC is 110 and the total enrolled to date at WRAMC is 110.

CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: Remote Management of the Critically Ill Patient Via Telecommunication

PRINCIPAL INVESTIGATOR: Popa, Christian MAJ, MC

ASSOCIATES: Thomas Fitzpatrick, COL, MC, and Thomas T Carmody, MAJ, MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: Critical Care Medicine Service

INITIAL APPROVAL DATE: 14 June 2001

### STUDY OBJECTIVE

1. Primary Objective: To demonstrate the feasibility of providing consultative services on critically ill patients from a remote site by specialty trained intensivists using telecommunication equipment. While the greatest potential application of providing consultative services via telecommunication will be at smaller community hospitals which do not employ critical care medicine physicians, we will test the system at an academic medical center (Walter Reed AMC Thoracic Intensive Care Unit) utilizing a critically ill patient population which does not receive routine consultative critical care services.

2. Secondary Objectives: a) To describe the clinical outcomes in critically ill patients who have received consultative services from a remote site by specialty trained intensivists using telecommunication equipment. b) To describe provider (nurse and physician) ratings of various aspects of remote monitoring using telemedicine, e.g., perceived value, level of comfort, satisfaction, and perceived quality of care.

### TECHNICAL APPROACH

This is a prospective trial that investigates the feasibility of providing critical care consultation using the Visicu system at some distance from the intensive care unit. The cohort consists of 300 post-operative patients convalescing in the Cardiothoracic ICU. The remote consultative service will be operational from 7 AM to 7 PM during the workweek. On a daily basis, an intensivist will make remote "morning rounds" on the patients from the monitoring station in conjunction with Cardiothoracic Surgery service morning rounds and offer management suggestions. He will then periodically reevaluate the patients as their medical condition dictates and be available by pager for additional management questions or issues from the surgeons. Intensivist, bedside nurse, surgical house staff, and attending surgeon satisfaction with and other responses to the remote monitoring system will be assessed using questionnaires. Technical data such as ease of establishing videoconferencing with the patient rooms, ability to visualize the patient, the infusion pumps, and the ventilator, and ability to contact the bedside nurse will also be tracked on a daily basis. Given the novelty of the equipment, the primary focus of this investigation will be to determine the feasibility and potential usefulness of remote intensive care management.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since receiving approval from DCI, the protocol underwent review and approval at HSRRB, Ft. Detrick. It then received final approval 12 February 2002. Since then, a retrospective chart review of the previous 200 Cardiothoracic ICU admissions has been completed to establish a control group for clinical outcome measurements. This has been completed and we are currently installing the last required piece of equipment in the electronic ICU, a CIS terminal for access to the electronic medical record. We have enrolled four patients in the previous year and have not enrolled new patients this year due to staffing changes and shortages due to events in Afghanistan and the Persian Gulf. We expect to re-start enrollment once things normalize and our physician and nursing staff return. Additionally, a related protocol involving remote consultation on ICU patients at Fort Belvoir has been submitted and is currently undergoing DCI review. A similar project to establish a telemedicine ICU link to Guam utilizing Visicu equipment is underway at Tripler Army Medical Center. There have been no recent literature developments which impact on either study design or patient safety. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

Ongoing study; no conclusions to date regarding feasibility of implementation in military facilities.

## DETAIL SUMMARY SHEET

**TITLE:** Does Oral Steroid Therapy After Tonsillectomy Decrease Postoperative Pain and Morbidity?  
A Prospective, Double-Blinded and Placebo Controlled Analysis

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** Battiata, Andrew CPT MC  
**ASSOCIATES:**

**DEPARTMENT:** Surgery

**STATUS:** C

**SERVICE:** Otolaryngology – Head and Neck

**INITIAL APPROVAL DATE:** 30 November 2000

### STUDY OBJECTIVE:

To determine if postoperative steroids following tonsillectomy will result in decreased morbidity and pain.

### TECHNICAL APPROACH

Prospective, double blinded placebo controlled trial. There have been no modifications of the technical approach.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

“Evaluating the effects of oral prednisolone on recovery after tonsillectomy – a prospective, double blind, randomized trial” is the only study published in Laryngoscope (December, 2000) on this issue. There was a notable shortcoming of the study, namely, the choice of the steroid and the dose of prednisone used. There was no statistical significant difference in postoperative pain and morbidity in the study group. To date, there have been no adverse events reported.

The number of subjects enrolled to the study since last APR at WRAMC is 3 and the total enrolled to date at WRAMC is 3.

### CONCLUSIONS

PI requests closure of study. This study is no longer actively enrolling patients.

## DETAIL SUMMARY SHEET

**TITLE:** A Phase III, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of Cevimeline in the Treatment of Xerostomia Secondary to Radiation Therapy for Cancer in the Head and Neck Region (Protocol 2011A-PRT003)

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** COL John Casler MC  
**ASSOCIATES:**

**DEPARTMENT:** Surgery

**STATUS:** O

**SERVICE:** Otolaryngology Head and Neck

**INITIAL APPROVAL DATE:** 24 July 2001

### STUDY OBJECTIVE

To determine the possible efficacy of Cevimeline in reducing the effects of radiation-induced xerostomia in patients who have been previously treated for head and neck cancer.

### TECHNICAL APPROACH

Prospective double-blinded randomization of active medication versus placebo. Patients are examined for improvement of xerostomia and salivary output is recorded.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Four additional patients enrolled since last APR. One patient withdrew because of logistical problems. One other stopped the medication because of diarrhea (which may have been viral). Adverse event problems have mainly been related to cholangitis. AE reports have been filed with DCI.

The number of subjects enrolled to the study since last APR at WRAMC is 4 and the total enrolled to date at WRAMC is 8. The total number enrolled study-wide is unknown, if multi-site study.

### CONCLUSIONS

The manufacturer is currently analyzing the data. No conclusions regarding efficacy have been published at this point.

## DETAIL SUMMARY SHEET

TITLE: In Vitro Gamma-Interferon Response to MTB Antigens in BCG-Vaccinated Individuals and Those with Equivocal PPD Skin Test Compared to Negative and Positive Control Subjects

PRINCIPAL INVESTIGATOR: Kim, Theodore MAJ MC  
ASSOCIATES:

DEPARTMENT: Allergy and Immunology  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 13 February 2001

### STUDY OBJECTIVE:

1) To see if subjects with equivocal PPD skin tests (>0 mm <10) will test positive or negative in an in vitro  $\gamma$ -interferon whole blood assay. 2) To see if positive levels of  $\gamma$ -interferon in negative PPD SKT subjects can predict PPD SKT conversion at a 6-month retest. 3) To compare the release of  $\gamma$ -interferon in an *in vitro* whole blood assay in subjects with equivocal PPD skin tests with those having positive PPD skin tests, with those having negative PPD skin tests, and with those having a history of BCG vaccination, using as stimulating antigens human PPD, avian PPD, Mycobacterium tuberculosis (MTB) culture filtrate fractions, or recombinant MTB antigens, singly and in combination. 4) To look at Th1/TH2 responses to the various MTB antigens in an *in vitro* cytokine flow cytometry assay.

### TECHNICAL APPROACH:

A PPD skin test is repeated on all subjects whose previous PPD test results are more than two months old. Blood samples obtained from each subject are incubated at 37°C for 20 hours with no antigen (phosphate buffered saline or PBS), the mitogen phytohemagglutinin (PHA), Human PPD, avian PPD, and a panel of specific MTB antigens, singly and in combination. These antigens include Antigen 85 complex and Mpt 32, Mpt 64, GrosES, GroEL, and ESAT 6. For the flow cytometry intracellular cytokine assay, whole blood is cultured with brefeldin A in addition to stimulating antigens in order to retain any cytokine produced in the intracellular space. Fluorescent-conjugated antibodies to Th1 type cytokines and cell-surface markers are used to measure the immune response to the antigens. These antibodies measure T-cell CD 69 activation and intracellular cytokine  $\gamma$ -IFN. The EIA immunoassay measures secretion of  $\gamma$ -IFN in whole blood culture in response to culture with the TB antigens. Plasma supernatants from the whole blood culture are harvested and frozen at -70°C until ready for the cytokine assay using the enzyme-linked immunoassay provided with the QuantiFERON kit.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The optimal concentrations of the specific MTB antigens were determined in preliminary dose/response experiments using the first five subjects in the positive and the negative groups. Although a detailed analysis of the raw data has not been conducted, the response of the MTB antigens GrosES and GroEL was higher than the other MTB antigens in the PPD skin test positive subjects. Including the preliminary dose/response subjects, a total of 83 patients have been enrolled in the study to date. The number of subjects enrolled in the study since last APR at WRAMC is 46.

Thus far, there have not been any adverse events. Also, there have been no patients withdrawn from the study.

### CONCLUSIONS

There are no conclusions to be made at this time.

## DETAIL SUMMARY SHEET

TITLE: Suppression of Ragweed Wheal Response by Montelukast - A Double-blind Study

KEYWORDS: ragweed, montelukast, skin testing

PRINCIPAL INVESTIGATOR: Waibel, Kirk H. CPT MC

ASSOCIATES: Martin, Bryan L. LTC(P)

DEPARTMENT: Allergy-Immunology

SERVICE:

STATUS: C

INITIAL APPROVAL DATE: 20 March 2001

### STUDY OBJECTIVE :

To see if the proportion of wheal reduction >50% during skin prick testing with ragweed in montelukast treated subjects (Group 1) will be different from the proportion of subjects in the placebo group (Group 2).

### TECHNICAL APPROACH:

The design was a prospective randomized double-blind study. Group 1 was designed to receive 10 mg of Montelukast by mouth once a day for seven days. Group 2 was designed to receive placebo for seven days. Below is a general outline of how the study was outlined.

Outline:	Time Allotment	Day#
1. Patient enrollment	1 hour	1
2. Initial skin testing	30 minutes	1
3. Study arm randomization	30 minutes	1
4. Repeat SPT 3hrs after first tablet	3 hours	1
5. Repeat SPT at one week	30 minutes	7
6. Patient finished with study	N/A	7

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Two patients were enrolled and skin tested initially. One of the patient's skin test was too small to meet the inclusion criteria for the study and was excluded from the study. The second patient completed three visits. No adverse events were reported.

The principal investigator relocated to another location and the associate investigator decided to close this study.

### CONCLUSIONS

No conclusions to date.



## DETAIL SUMMARY SHEET

TITLE: Visconsupplementation in the Treatment of Chondromalacia Patellae

PRINCIPAL INVESTIGATOR: Roebuck, Jonathan D. CPT MC

DEPARTMENT: Medicine

STATUS: C

SERVICE: Rheumatology

INITIAL APPROVAL DATE: 20 February 2001

### STUDY OBJECTIVE:

1. To compare the mean difference in the degree of knee pain between two groups of subjects that receive either viscosupplementation or placebo for the treatment of chondromalacia patella. 2. To compare the mean difference in the functional status between two groups of subjects that receive either viscosupplementation or placebo in the treatment of chondromalacia patella.

### TECHNICAL APPROACH:

1. Initial evaluation for clinical signs/symptoms of chondromalacia patella (CMP): patellar apprehension, pain, disability (standard of care).
2. Rule out exclusionary criteria; rule in inclusionary (research).
3. Consent patients to the study (research).
4. Randomize patients to aforementioned treatment arms (research): Control (standard therapy plus placebo) or Treatment (standard therapy plus viscosupplementation).
5. See subjects once a week for 3 weeks to inject either SYNVISIC or placebo into the affected knee (as described in detail in the background section above).
6. Follow up evaluation with physical exam and data collection questionnaires at 3-month intervals for 6 months (research).
7. Questionnaires will be filled out on three separate occasions for each patient in the treatment and control groups; first at enrollment, then at each of the 3 month follow up visits. The questionnaire includes pain inquiries with visual analog scale for many measures according to the Western Ontario McMaster University osteoarthritis index (WOMAC) score as well as determinants of functional status by Lequesne's index and WOMAC scores.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE:

Unfortunately, this project has lost steam and interest from both referring specialties and (probably most importantly) the drug manufacturer for the indication that was proposed. It is with reluctance that PI requests this protocol be closed. Thanks to all involved.

The number of subjects enrolled to the study since last APR at WRAMC is N/A and the total enrolled to date at WRAMC is N/A.

### CONCLUSIONS:

None.

## DETAIL SUMMARY SHEET

TITLE: ACRIN 6651 - Role of Radiology in the Pretreatment Evaluation of Invasive Cervical Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC

ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology

STATUS: O

SERVICE: Gynecologic Oncology Group

INITIAL APPROVAL DATE: 21 November 2000

### STUDY OBJECTIVE

This study is to determine the usefulness of modern imaging in diagnosing and evaluating cervical cancer. Specifically, to see how accurate imaging is when it is compared to surgical findings, and if in the future modern imaging can represent a "one-stop shop" before making treatment decisions in patients with newly diagnosed cancer of the cervix.

### TECHNICAL APPROACH

Patients with documented cervical cancer and clinical FIGO Stage IB1 and tumor size >2cm, Stage IB2, and greater, who are scheduled for surgery, will be imaged preoperatively with CT and MRI.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is N/A and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 110, if multi-site study.

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: GOG 0179 - A Randomized Phase III Study of Cisplatin vs. Cisplatin Plus Topotecan vs. MVAC in Stage IVB Recurrent or Persistent Carcinoma of the Cervix

KEYWORDS:

PRINCIPAL INVESTIGATOR: LTC G. Scott Rose MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 17 April 2001

### STUDY OBJECTIVE

The first purpose is to determine if combination of cisplatin and topotecan or MVAC are better than cisplatin alone in the treatment of advanced or recurrent cervical cancer. The second purpose is to compare side effects and health-related quality of life between the three treatments.

### TECHNICAL APPROACH

For patients with advanced, persistent or recurrent squamous cell carcinoma of the cervix no longer amenable to surgical resection or radiation therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this is the first review for this study, there have been no publications reporting data from studies with similar study design in the literature. The objectives of this investigation have not been fulfilled by prior studies.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 364, if multi-site study. Grade 4 toxicities are 24 WBC, 9 hemoglobin, 4 platelets, 51 granulocytes, 4 other hematologic, 1 allergy/immunology, 5 other cardiovascular, 1 coagulation, 1 constitutional, 2 nausea, 2 vomiting, 6 other GI, 12 genitourinary, 2 hemorrhage, 2 infection, 4 metabolic, 1 musculoskeletal, 3 other neurologic, 9 other pain, and 2 pulmonary. Grade 5 toxicities include 2 pulmonary.

Ref: Jan 03 GOG Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: GOG 0184 - A Randomized Phase III Study of Tumor Volume Directed Pelvic Plus or Minus Para-Aortic Irradiation Followed by Cisplatin and Doxorubicin or Cisplatin, Doxorubicin and Paclitaxel for Advanced Endometrial Carcinoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: LTC G. Scott Rose MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 24 April 2001

### STUDY OBJECTIVE

To compare treatment outcomes (survival and progression-free survival) in patients with Stage III-IV endometrial carcinoma ( $\leq 2$  cm residual disease) treated with tumor volume directed pelvic plus or minus para-aortic irradiation followed by cisplatin and doxorubicin or cisplatin, doxorubicin and paclitaxel chemotherapy. Compared short and long-term toxicities between the chemotherapy regimens.

### TECHNICAL APPROACH

All patients with advanced endometrial carcinoma, of any histology, including clear cell and serous papillary carcinomas.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 3 and the total enrolled to date at WRAMC is 3. The total number enrolled study-wide is 397, if multi-site study. Grade 4 toxicities include 61 WBC, 3 platelets, 81 ANC/AGC, 1 other hematologic, 1 cardiovascular, 2 constitutional, 1 nausea, 1 gastrointestinal-other, 1 hemorrhage, 1 infection-other, 2 metabolic, 1 neurologic-other.

Ref: Jan 03 GOG Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: GOG 0182 - A Phase III Randomized Trial of Paclitaxel and Carboplatin Versus Triplet of Sequential Doublet Combinations in Patients with Epithelial Ovarian or Primary Peritoneal Carcinoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: LTC G. Scott Rose, MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 15 May 2001

### STUDY OBJECTIVE

To compare the efficacy of each experimental arm with the control arm (paclitaxel and carboplatin). Efficacy will be determined through analysis of overall survival (OS) and progression-free survival (PFS). A single interim analysis based on PFS will be performed to select promising arms for full accrual.

### TECHNICAL APPROACH

This is a Phase III randomized trial of paclitaxel and carboplatin versus three drugs given at the same time or two drugs given at the same time in patients with epithelial ovarian or primary peritoneal cancer. Modifications to this study include clarification of the order of drugs given and clarification of method of creatine clearance testing.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data from studies with similar study design in the literature. The number of subjects enrolled to the study since last APR at WRAMC is 5 and the total enrolled to date at WRAMC is 12. The total number enrolled study-wide is 2,146, if multi-site study.

Grade 4 toxicities are broken down by Arm (A, B, C, D, and E). They include: WBC- 15A/50B/48C/15D/16E; HGB-1A/6B/3C/2D/7E; Platelets- 5A/27B/12C/15D/20E; Granulocytes- 142A/170B/170C/144D/120E; Other Hematologic-2B/1D/1E; Allergy- 4A/1C/2D/1E; Cardiovascular- 2A/4B/4C/1D/5E; Coagulation- 1B/1E; Constitution- 2B/4C/2D/1E; Dermatologic- 1C; Gastrointestinal- 5A/6B/3C/2D/3E; Genitourinary- 2A/1B/1D/2E; Hemorrhage- 1A/1B/1E; Infection/Fever- 4A/4B/2C/1D/3E; Metabolic- 2A/1B/1D/5E; Musculoskeletal- 1D; Neurologic- 2A/1B/1C/2E; Peripheral Neurologic- 1B/1C; Pain- 1B/1D; Pulmonary- 3A/2C/2D/2D.

Grade 5 toxicities included (by Arm): Platelets-1E; Cardiovascular- 1B/5C/2E; Constitution- 1B; Gastrointestinal- 1A/1C/1D; Genitourinary- 1E; Hemorrhage- 1E; Hepatic- 1B; Infection/Fever- 2A/1B/1C/3D/1E.

### CONCLUSIONS

A preliminary review of dose-limiting toxicity, adverse event reports, and treatment delivery confirms the feasibility of each regimen as written. Accrual on all five arms continues pending interim analysis.

## DETAIL SUMMARY SHEET

TITLE: GOG 0189 - Randomized Phase III Crossover Trial of Chemotherapy (Doxorubicin/Cisplatin/Paclitaxel and G-CSF) vs. Hormonal Therapy (Tamoxifen/Megestrol Acetate) in Patients with Stage III & IV or Recurrent Endometrial Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: LTC G. Scott Rose, MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: C  
INITIAL APPROVAL DATE: 15 May 2001

### STUDY OBJECTIVE

To determine if combination doxorubicin, cisplatin (TAP), and paclitaxel chemotherapy improved progression-free survival and response when compared to hormonal therapy. To determine if the sequence of treatments, alternating megestrol acetate and tamoxifen (MAT) hormone therapy, or TAP chemotherapy, affects survival. To determine if progesterone receptor status provides information on whether a patient is more likely to benefit from TAP chemotherapy.

### TECHNICAL APPROACH

The patient has been diagnosed with endometrial cancer that cannot be cured with surgery or radiation therapy. The patient will be randomized to receive one of two treatments that will also include a crossover design to assess the effect of therapy sequence on overall survival.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data from studies with similar study design in literature.

This study was closed to patient accrual on 12 August 2002. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 48. There is no information regarding Grade 4 toxicities.

### CONCLUSIONS

None. This study was closed on 12 Aug 2002 due to inadequate patient accrual.

## DETAIL SUMMARY SHEET

TITLE: Creation of a Tissue Library for the Study of Molecular Carcinogenesis in Gynecologic Malignancies

KEYWORDS:

PRINCIPAL INVESTIGATOR: Maxwell, G. Larry MAJ MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecology Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 21 November 2000

### STUDY OBJECTIVE:

Create a tissue bank of uterine fibroids to facilitate the investigation of characteristic molecular alterations. Collect normal DNA from myometrium and blood cells in addition to uterine fibroids to facilitate genetic analysis. Develop primary and immortalized cell cultures from uterine leiomyomata specimens.

### TECHNICAL APPROACH

Patients who present to the WRAMC GYN Oncology division and are found to require surgery for uterine leiomyomas will be considered eligible for participation in this protocol during the first year of activation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data from this study or others with similar study design. Adverse effects are not applicable since this is a tissue procurement study.

The number of subjects enrolled to the study since last APR at WRAMC is 14 and the total enrolled to date at WRAMC is 18.

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

**TITLE:** The Comparison of the Effectiveness of Burch Colposuspension Versus Suburethral Sling in the Management of Primary Genuine Stress Urinary Incontinence

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** LT Nicole Carlson, MC, USN

**ASSOCIATES:** LTC Ernest G. Lockrow, DO; Burkhardt H. Zorn MD

**DEPARTMENT:** Obstetrics and Gynecology

**SERVICE:** Gynecology

**STATUS:** C

**INITIAL APPROVAL DATE:** 9 January 2001

### STUDY OBJECTIVE:

Compare the success and complications of two procedures (suburethral sling vs. Burch Retropubic Urethropey) currently used for the treatment of primary genuine stress urinary incontinence.

### TECHNICAL APPROACH:

This is a retrospective cohort study. Information will be gathered from chart review with further information gathered from patients through the use of a survey. Patients will have had either a Burch urethropey or suburethral sling and will have met selection criteria with consent given for participation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A retrospective chart review of 150 patients undergoing either Burch retropubic urethropey or suburethral sling for the treatment of incontinence between 1995 and 1999 was conducted. There were 33 subjects in the Burch group, and 27 in the sling group that met the selection criteria. Subjects were selected based on the inclusion criteria. Between January 1995 and December 1999, 150 patients underwent either a Burch or sling procedure in our institution. Seventy-four patients had a primary incontinence procedure, and of those, 33 Burch urethropey and 27 sling procedures met the selection criteria. Questionnaires were sent out to all sixty of the study subjects, with a return rate of 48%. Sixteen patients from the Burch group, and thirteen from the sling group, returned the questionnaire instrument. The sling group was slightly older than the Burch group (55.11 vs. 49.67 years,  $p=0.11$ ). Height and weight were comparable in both groups. Hormone replacement therapy was slightly higher in the sling group (63.0% vs. 48.5%,  $p=0.31$ ). Estimated blood loss and surgery complications, length of surgery, and concomitant procedures were higher in the Burch group, and were statistically significant as compared to the sling group. Success of the procedure as measured by subjective questionnaire of no urine leak was slightly better in the Burch group in comparison to the sling (62.5% vs. 53.8% respectively,  $p=0.64$ ). Urge incontinence as defined by the subjective response was comparable to other studies (63% in the Burch group and 15.4% in the sling group,  $p=0.28$ ). Average length of follow-up for those patients responding to the questionnaire was 4.5 years in the Burch group range (2.0-6.5 years) and 4 years in the sling group range (2.0-5.5 years). There were no adverse events during the study. The number of subjects enrolled to the study since last APR at WRAMC is 150 and the total enrolled to date at WRAMC is 150.

### CONCLUSIONS

In our patient population, we found no difference in the success rate of the Burch vs. the sling procedure when used in patients as the primary procedure for the correction of genuine urinary stress incontinence. When comparing the two groups, we found a statistically significant difference in the length of surgery, estimated blood loss, and transfusion rate. When patients with hysterectomy were removed, there was only a significant difference shown in surgical times. Otherwise, there was no difference between the two procedures. In our institution, the Burch urethropey is as good, if not better, than the sling procedure for the treatment of primary stress incontinence. We agree with other authors that there is a need for comparative prospective studies to determine the optimal operation for primary incontinence.



## DETAIL SUMMARY SHEET

TITLE: Creation of a Tissue Library for the Study of Molecular Alterations Characteristic of Uterine Leiomyomata

KEYWORDS:

PRINCIPAL INVESTIGATOR: Maxwell, G. Larry, MAJ, MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 20 February 2001

### STUDY OBJECTIVE

1. Create a tissue bank of uterine fibroids to facilitate the investigation of characteristic molecular alterations.
2. Collect normal DNA from myometrium and blood cells in addition to uterine fibroids to facilitate genetic analysis.
3. Develop primary and immortalized cell cultures from uterine leiomyomata specimens.

### TECHNICAL APPROACH

Following completion of the hysterectomy, the surgeon will accompany the specimen to the anatomic pathology unit in order to obtain tissue samples for the bank.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No publications have resulted from this study or studies with similar study design. The objectives of this investigation have not been fulfilled by prior studies. One study based on tissue from this bank is pending approval at DCI. There have been no adverse events to report on this study.

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: An Observational Trial To Evaluate Tissue and Peripheral Immune Response to HPV 16-Induced Cervical Intraepithelial Neoplasia

PRINCIPAL INVESTIGATOR: Rodriguez, Mildred, LCDR, MC, USN  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 19 June 2001

### STUDY OBJECTIVE

This is an observational study evaluating tissue and peripheral blood assays of endogenous immune response to cervical infection with human papilloma virus (HPV) 16, in correlation with clinical, histological, and virologic evaluation. No investigation therapy will be involved. All patients will receive state-of-the-art diagnostic and therapeutic care. This information will lay the groundwork for the responses, which will be evaluated in subsequent vaccine trials. The overall goal of this initial study is to characterize the immune response to cervical precursor lesions.

1. To characterize local tissue response to high-grade cervical intraepithelial lesions.
2. To characterize peripheral measures of immune response in patients with high-grade cervical intraepithelial lesions.
3. To correlate these assays of immune response with known clinical, histopathologic, and virologic prognostic features of HPV-induced disease.

The secondary objectives of this study are:

1. To estimate person-to-person variations in clinical endpoints including change in lesion size and change in viral load.
2. To characterize the magnitude of change attributable to standard of care in these endpoints.
3. To estimate the within person variability of these measures over the course of the observation period.

### TECHNICAL APPROACH

The technical approach involves understanding how the immune system reacts to the pre-cancerous changes and to a virus called HPV 16 (human papilloma virus) that may be causing the pre-cancerous changes. Swabs of the cervix and blood tests will be performed to see how many HPV 16 viruses are present in the cervix and to look at special blood cells that are part of the immune system. Cervical tissue removed for biopsies or treatment of the pre-cancerous changes will also be analyzed to look for special cells that are part of the immune system. The results of this study will be used to decide which immune responses will be looked at in the future.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data from studies with similar study design in the literature. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. Of eighty patients consented for participation at Johns Hopkins University, there are 16 evaluable patients to date. No toxicities to report.

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: Intraoperative Staging of Lung Cancer Using the Gamma Probe and Tc-99m Depreotide

KEYWORDS:

PRINCIPAL INVESTIGATOR: Bridwell, R.S. MAJ MC

ASSOCIATES: Mulligan, C.; Montilla, J.

DEPARTMENT: Radiology

SERVICE: Nuclear Medicine

STATUS: O

INITIAL APPROVAL DATE: 12 December 2000

### STUDY OBJECTIVE

To evaluate the use of Tc-99m depreotide with the intraoperative gamma probe in patients undergoing thoracotomy for the staging of lung cancer. Objectives that will be realized within the scope of staging using Tc-99m depreotide are:

1. Correlate the imaging findings with anatomical pathology.
2. Correlate findings on conventional imaging to Tc-99m depreotide.
3. Develop quantitative imaging region of interest and correlate with anatomical pathology.
4. Correlate the quantitative ROI system, visual study interpretation to the intraoperative gamma probe reading from sampled tissue that have been removed from the subject at time of surgery.
5. Correlate the gamma probe findings to nodal anatomical pathology examination.
6. Correlate the stage found by quantitative imaging techniques to anatomical pathology stage.

### TECHNICAL APPROACH

This is a prospective observational study comparing the gamma probe counts of lymph node tissue removed from the body after injection with Technetium 99m depreotide with anatomical pathology in patients undergoing staging operative procedures for lung cancer. There have been no modifications since the study started.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

To date there have been six patients enrolled. Three of the six patients did not complete the study due to terrorist attack and power outage, respectively. There have been no adverse events in the six patients that have been enrolled in the study.

The number of subjects enrolled to the study since last APR at WRAMC is 13 and the total enrolled to date at WRAMC is 19.

### CONCLUSIONS

This study is ongoing and enrollment continues. There have been two abstracts submitted. One was accepted at the European Nuclear Medicine Conference in Vienna in August. The other is pending acceptance by one of the co-investigators.

## DETAIL SUMMARY SHEET

TITLE: Preoperative Evaluation of Breast Carcinoma Utilizing Tc99m-Depreotide

PRINCIPAL INVESTIGATOR: MAJ Jaime L. Montilla-Soler, MC

ASSOCIATES:

DEPARTMENT: Radiology  
SERVICE: Nuclear Medicine

STATUS: O  
INITIAL APPROVAL DATE: 15 May 2001

### STUDY OBJECTIVE

To evaluate the preoperative diagnostic utility of a new FDA approved polypeptide, Tc99m-depreotide (NeoTect) that targets somatostatin receptors 2, 3, and 5 for the detection of breast carcinoma.

### TECHNICAL APPROACH

Nuclear Medicine:

Injection and imaging of Technetium 99m-depreotide:

Technetium 99m-depreotide is a commercially available, FDA approved radiopharmaceutical for the evaluation of solitary pulmonary nodules at risk for primary lung carcinoma. The radiopharmaceutical is available in kit form and is formulated on site in our nuclear pharmacy. Each vial will be made per approved standard operating procedures and assayed for radiochemical purity using saturated sodium chloride solution prior to injection into the subject. The radiopharmaceutical, after being prepared and passing quality assurance testing, will be injected into the subject using an intravenous route of administration. The intravenous injection will be administered in the contralateral arm with respect to the affected breast. Twenty millicuries (20 mCi) of Technetium 99m-depreotide will be used for each subject. Two hours after injection the subject will be imaged utilizing a standard gamma camera. Two cameras approved for nuclear imaging will be utilized for this study: the BIAID (Trionix Corporation, Twinsburg, Ohio) and the XLI SMV (SMV corporation, Twinsburg, Ohio). Imaging will be performed using planar and SPECT (single photon emission tomography) techniques with the patient placed in the prone position using the scintimammography table adapter.

Planar images of the chest will be obtained in the anterior and lateral projections with the patient placed in a prone position using the mammography table insert with breast cutouts and the arms raised with the hands positioned on the head. SPECT images of the head, neck and chest to include the breasts will be performed in the same position. The SPECT acquisition images will be acquired using a step and shoot protocol (45 steps, 4 degrees per step, 30 seconds per stop), 128 X 128 matrix, and a low energy high-resolution collimator. The energy window will be centered at 140 keV. Regions of interest (ROI) will be drawn around the areas of abnormal accumulation of the radiotracer within the breast as well as around a comparable area size in the unaffected breast. If no clearly defined abnormal uptake is seen, an ROI of the upper outer quadrants will be used to calculate an uptake ratio, with the 'abnormal' side determined after review of the patient's history. The region of interest data will be tabulated for statistical evaluation to determine a normal vs. abnormal uptake ratio value within a breast abnormality when compared to the anatomical pathology results. Images will be reviewed by at least two board certified nuclear medicine physicians. The initial exam interpretation will consist of a blinded interpretation, without the benefit of any clinical history, physical examination or clinical stage of the patient as determined by the oncologic surgeon. This exam interpretation will be rendered as a positive/negative examination for abnormal breast radiotracer accumulation. Subsequently, the interpreting physician will be provided with the clinical information as well any anatomical/radiological information available and a second exam interpretation will be performed. The purpose of this second interpretation with the benefit of clinical data is to provide the interpreting physician with the benefit of comparing the normal vs. the suspected abnormal breast as well as for accurate selection and determination of Regions of Interest in the suspicious breast quadrant to compare with the normal breast. This information will be recorded on the nuclear medicine data collection forms. If there is disagreement between the two physicians, a

third board certified nuclear medicine physician will be employed and a consensus achieved. Recording of the abnormalities will be performed on a data collection sheet and printed for review.

**Surgery:**

Surgical procedures will be performed as per standard of care. The surgery will take place more than 24 hours after the injection of Technetium 99m-depreotide. A 24-hour window is desired, since the target population is also eligible for gamma probe assisted sentinel node biopsy at the time of surgery. The 24-hour window is required to preserve the eligibility of these patients for the gamma probe assisted sentinel node biopsy procedure. After initial survey the surgeon will fill out a form identifying suspicious sites on a data collection form. Identification of the primary cancer location will be obtained. Sampling of tissue will be performed per standard of care and directed by conventional imaging and clinical criteria. The surgeon on a data collection form will identify sampled tissue. The attending surgeon will not have knowledge of the Tc99m-depreotide scintimammography results prior to the surgery. Results obtained from the Tc99m-depreotide scintimammography will not alter patient care.

**Specimen treatment:**

Samples will undergo routine pathologic evaluation. This includes histological evaluation of the breast tissue as well as tissue marker evaluation, specifically determination of HER and NEU marker positive/negative status, which is part of our standard pathological evaluation at our institution. No additional histological evaluation or different tissue handling from the standard pathology department's SOP will be required in this study. The nuclear medicine imaging results will be compared to the standard pathological evaluation results rendered as a pathology report on this hospital's medical information system (CHCS). The pathology results that the protocol will be looking at include the presence or absence of breast cancer (positive or negative histology) as well as the histology type of the breast tissue obtained for pathological evaluation.

**PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE**

Total enrollment to date: 21 patients.

Amendments or modifications: None.

Sensitivity to date: 95%

Specificity to date: 99%

Our research suggests that this radiotracer is very sensitive and specific for the presence of breast carcinoma as well as for the detection of early metastatic disease. The number of subjects enrolled to the study since last APR at WRAMC is 16. The total enrolled to date at WRAMC is 21. The total number enrolled study-wide is 21.

**CONCLUSIONS**

This radiotracer is very sensitive and specific for the diagnosis of breast carcinoma. Our patient population thus far is small, secondary to other current events that affect how health care is being provided at WRAMC. Availability of the product has been an issue since November 2002, secondary to a production difficulty at Berlex labs in Germany. The product has not been available in the U.S. since then. As soon as production resumes, we will be able to continue patient enrollment.

## DETAIL SUMMARY SHEET

TITLE: Evaluation of Intra-prostatic Radio-opaque Markers for Prostate Localization and Refinement of External Beam Treatment Techniques

KEYWORDS:

PRINCIPAL INVESTIGATOR: MAJ William B. Warlick MC

ASSOCIATES: MAJ Michael Dullea; COL Judd Moul MC

DEPARTMENT: Radiology

STATUS: C

SERVICE: Radiation Therapy

INITIAL APPROVAL DATE: 16 January 2001

STUDY OBJECTIVE:

The objectives of the study are: 1) to quantify the movement of marker seeds within the prostate during a course of radiation therapy and 2) to measure any movement of the prostate in reference to the initial planning CT scan over a course of radiation therapy.

TECHNICAL APPROACH:

We are still following the same approach as described in the original protocol. We place the marker seeds as an outpatient procedure in the Urology clinic. This procedure has been well tolerated. We then proceed with standard radiation planning followed by standard radiation treatments. We also take additional weekly diagnostic quality x rays for seed location and measurements as well as a repeat CT scan in week 4 and week 7 of the radiation treatments for prostate position.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT

The participation by patients has been good. The patients have tolerated the placement of the seeds well. There have been no side effects other than minor bleeding at the time of the procedure. During the course of radiation treatments, there have been no unexpected side effects. Currently, three patients have experienced Grade 1 acute urinary toxicity (increased urinary frequency and urgency). One patient experienced Grade 2 acute urinary toxicity (hematuria) and two patients experienced Grade 2 acute urinary toxicity (frequency/urgency requiring medications). Three patients experienced Grade 1 acute GI toxicity (change in bowel habits not requiring medications). These side effects are similar to our patients undergoing standard radiation treatments. There have been no new advancements that would impact upon the treatment of these patients.

The number of subjects enrolled to the study since last APR at WRAMC is 9 and the total enrolled to date at WRAMC is 9.

CONCLUSIONS

This study has been closed to accrual, and the data is currently in the process of being published.

## DETAIL SUMMARY SHEET

**TITLE:** A Prospective Study of Outcomes of Patients Examined with Electron Beam Computed Tomography of The Coronary Arteries

**KEYWORDS:** Coronary, calcinosis, EBCT, calcium, tomography

**PRINCIPAL INVESTIGATOR:** Feuerstein, Irwin MD DAC

**ASSOCIATES:** COL M. Brazaitis MC, Dr. S. Greberman, Dr. M. Greberman, COL J. Zoltick MC

**DEPARTMENT:** Radiology

**STATUS:** C

**SERVICE:** Diagnostic Radiology

**INITIAL APPROVAL DATE:** 21 November 2000

### STUDY OBJECTIVE:

To collect clinical data on patients examined with electron beam computed tomography (EBCT) of the coronary arteries. To collect follow-up information of medical history subsequent to the EBCT. To analyze patient demographics, calcium score distributions, and treatment outcomes.

### TECHNICAL APPROACH

This is a database and survey protocol. Anonymous clinical data and laboratory results will be entered into a research database. Patients will be sent outcome questionnaires yearly for five years, and the data analyzed. This is considered a minimal risk protocol. The only changes in the protocol have been the separation of prospective and retrospective portions, and the questionnaire changed in format and was submitted as part of the review process. An advertisement letter was submitted.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 9 and the total enrolled to date at WRAMC is 741.

### CONCLUSIONS

This study is being closed due to insufficient resources and extensive damage to the EBCT section from flooding of potentially hazardous material.

## DETAIL SUMMARY SHEET

TITLE: Postmenopausal Coronary Artery Disease and Osteoporosis - A Pilot Study

KEYWORDS: osteoporosis, coronary artery disease, spine, computed tomography, bone densitometry

PRINCIPAL INVESTIGATOR: Feuerstein, Irwin MD

ASSOCIATES: Sharyn Greberman, Abby Rogers, Robert Vigersky, Susan Dunlow, Michael Brazaitis

DEPARTMENT: Radiology

STATUS: O

SERVICE: Diagnostic Radiology

INITIAL APPROVAL DATE: 17 April 2001

### STUDY OBJECTIVE:

There have been no changes to the study objectives, which remain as follows. The overall goal of this protocol is to evaluate combined radiologic evaluation for coronary artery disease (CAD) and osteoporosis in postmenopausal women. Subgoals include evaluating the relationship between CAD and osteoporosis, and comparing osteoporosis evaluation in the thoracic and lumbar spines. This information will be used to develop and evaluate a high-quality, one-step technique for the evaluation of coronary artery calcium (CAC) and bone mineral density (BMD) using electron beam computed tomography (EBCT). A further subgoal is to validate the measurement of thoracic spine bone density with Dual Energy X ray Absorptiometry (DEXA).

### TECHNICAL APPROACH:

This pilot study will be conducted for a one-year period in fifty postmenopausal women.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no significant changes in the procedures or in the literature regarding performance and interpretation of the study procedure. Data analysis is ongoing. There are no study findings that are reportable at this time. They should be available in the next few months. There was one protocol deviation reported last month that was reviewed by the Human Use Committee. This patient has been excluded from the protocol, and a single additional patient has been enrolled, taking the study population back to fifty patients. The program was audited once, with no significant problems identified.

The number of subjects enrolled to the study since last APR at WRAMC is 11 and the total enrolled to date at WRAMC is 50.

### CONCLUSIONS:

Enrollment is closed. Data analysis is ongoing.



## DETAIL SUMMARY SHEET

TITLE: Use of Robotic Telepathology as an Adjunct to Frozen Section Consultation

KEYWORDS: Telepathology, frozen section, diagnosis, AFIP

PRINCIPAL INVESTIGATOR: Kaplan, Keith MAJ MC

ASSOCIATES: Myers, Cris P. COL MC

DEPARTMENT: Pathology and Area Laboratories

STATUS: C

SERVICE:

INITIAL APPROVAL DATE: 13 March 2001

### STUDY OBJECTIVE

To assess the validity and feasibility of remote, real-time telepathology consultation for frozen section (intraoperative consultation) in the AMEDD.

### TECHNICAL APPROACH

Method and study design as proposed.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study completed per study design as proposed with 120 cases reviewed in a retrospective fashion.  
Publication clearance (Database #7383) 20 December 2002.

The total number enrolled study-wide is 120 if multi-site study.

### CONCLUSIONS

Use of telepathology proved to provide support for pathologists located at distant sites.

## DETAIL SUMMARY SHEET

TITLE: An Archival Fixed Tissue Thyroid Tissue Bank

KEYWORDS: thyroid, cancer, IGF

PRINCIPAL INVESTIGATOR: Gary Francis COL MC

ASSOCIATES: Andrew Bauer, Aneeta Patel, Michael Tuttle

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Endocrinology

INITIAL APPROVAL DATE: 3 April 2001

### STUDY OBJECTIVE

To determine genes that are expressed by thyroid cancers and to determine if gene expression has an impact on the clinical behavior of individual tumors.

### TECHNICAL APPROACH

Archival, formalin fixed thyroid tumors will be sectioned and stained for various macromolecules. The intensity of staining will be quantified and correlated with tumor size, extent of disease, and recurrence.

### PRIOR AND CURRENT PROGRESS

We have successfully stained many of these thyroid cancers for expression of a variety of macromolecules that have proven to have an impact on the clinical behavior of thyroid cancers.

The number of subjects enrolled to the study since last APR at WRAMC is 400 and the total enrolled to date at WRAMC is 400. The total number enrolled study-wide is 400, if multi-site study.

### CONCLUSIONS:

Expression of several important macromolecules have been shown to be important in the clinical behavior of thyroid cancers. The tissue bank is indispensable in continuing this productive line of work.

## DETAIL SUMMARY SHEET

TITLE: The Role Of Caveolin-1 in Thyroid Carcinoma

KEYWORDS: Thyroid cancer, caveolin-1, benign thyroid tumors

PRINCIPAL INVESTIGATOR: Powers, Patricia COL MC

ASSOCIATES: Gary L. Francis, Catherine Dinauer, Andrew Bauer, Henry Burch, Yvonne Lukes, Diarmuid Nicholson, Maged Abdel-Rahim

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Endocrinology

INITIAL APPROVAL DATE: 10 April 2001

### STUDY OBJECTIVE:

To improve our understanding of the molecular biology of thyroid cancer and how individual mutations or expressed protein products determine the clinical course of individual tumors. In the first part of this sub-study, we plan to determine if thyroid cancers that express caveolin-1 behave differently from thyroid cancers that do not express caveolin-1, and if benign lesions express caveolin-1 differently from malignant tumors. In the second part of the study, we plan to investigate the effect of angiogenesis stimulators and inhibitors on caveolin-1 expression in cell cultures.

### TECHNICAL APPROACH

PART 1: The Expression of Caveolin-1 in Archived Thyroid Cancer Tissue Blocks

Subjects: This protocol will use only previously existing, archived thyroid tissues/slides and the corresponding clinical data-domains outlined in the "master protocol" WU# 01-65001, entitled "An Archival Fixed-Thyroid Tissue Bank". The final number of materials available for this sub-study will vary slightly but will not exceed 200 adult tumors, 70 pediatric tumors, 50 benign thyroid lesions, and 75 radiation induced tumors.

Study Design: This proposal is an observational, retrospective analysis of caveolin-1 expression among a group of diverse thyroid tumors. Caveolin-1 expression will be determined by immunohistochemistry and correlated with the clinical data domains outlined above. The results of caveolin-1 expression will be entered into a computerized database that includes the patient age and gender; tumor histology, size, and extent of disease at diagnosis; as well as the treatment and outcome for each individual patient. A corresponding random unique number identifies the tissue block and the database domains so that the result of the caveolin-1 testing can be correlated with the clinical history. However, neither the database nor the tissue blocks contain any patient name, number, or pathology number. By this means, no patient can be identified from either the tissue or the database. No patient will be contacted for this study, and no new patients will be recruited. Only the previously existing, archived materials already in the laboratory will be used. Thyroid tissue sections will be stained for the expression of caveolin-1 by immunohistochemistry.

PART 2: The Effect of Angiogenesis Stimuli and Inhibitors on the Expression of Caveolin-1 by Thyroid Cell Cultures: We will use cell cultures to directly examine the effect of angiogenesis stimulators and inhibitors on *in vitro* caveolin-1 expression. The cell cultures to be used include ARO, WRO and NPA thyroid cancer cells. They were commercially obtained and the identity of the original patients from which they were obtained cannot be traced. Caveolin-1 expression will be determined by two methods - Western blot analysis of protein expression and RT-PCR determination of caveolin-1 mRNA production. Both methods will be used to determine if there is an effect at the transcription level (mRNA) or protein level (Western blot).

By studying the role of caveolin-1 in all three cell types, we will be able to determine if caveolin-1 expression is lost from anaplastic thyroid cancer (ARO), but retained by differentiated thyroid cancer (NPA). If so, this will allow caveolin-1 immunostaining to be used to help distinguish the level of tumor differentiation. We will then examine

Work Unit # 01-65001a [*Continued*]

the direct effect of several of the more common angiogenic stimuli [vascular endothelial growth factor (VEGF), platelet derived growth factor (PDGF), epidermal growth factor (EGF), and basic fibroblast growth factor (bFGF)] on the expression of caveolin-1 by each of these cell lines. The results of these experiments will directly determine if caveolin-1 expression is modulated by angiogenic stimuli in thyroid cancers. We will also examine the effect of angiogenesis inhibitors on caveolin-1 expression. We plan to study the effect of anti-VEGF antibody and thalidomide using all three-cell cultures. The intensity of caveolin-1 expression for each treatment will be compared to the control cultures. The intensity of caveolin-1 expression will be determined by scanning and densitometric analysis of the appropriate bands (NIH Image). Each experiment will be repeated three times to ensure any observed effect is replicable. There have been no modifications to the original methodology.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

We have purchased materials and stained 30 archived tissue blocks as described in Part 1, but because PI's prolonged absence last fall, we have not completed analysis of these. We have not yet begun Part 2. No recent literature to summarize. No amendments or modifications to the study since its approval.

The number of subjects enrolled to the study since last APR at WRAMC is N/A and the total enrolled to date at WRAMC is N/A.

CONCLUSIONS

None yet.

## DETAIL SUMMARY SHEET

**TITLE:** Pre-clinical Pilot Study to Determine if the Novel Tumor-Activated Fluoropyrimidine Carbamate Capecitabine (Xeloda®, Hoffman-Laroche, Inc.) Could be Used to Treat Thyroid Carcinoma: Are Cytidine Deaminase, Thymidine Phosphorylase (TP), Dihydropyrimidine Dehydrogenase (DPD), and Thymidylate Synthase (TS) Present in Thyroid Carcinoma?

**KEYWORDS:** Xeloda, Pilot Study

**PRINCIPAL INVESTIGATOR:** Andrew J. Bauer, MAJ, MC

**ASSOCIATES:** Henry Burch COL MC USA; Patricia Powers COL MC USA; Gary Francis COL MC USA

**DEPARTMENT:** Pediatrics

**STATUS:** O

**SERVICE:** Pediatric Endocrinology

**INITIAL APPROVAL DATE:** 14 September 2001

### STUDY OBJECTIVE:

Pilot study to determine if various forms of thyroid cancer express enzymes that would predict if the novel-tumor activated 5-FU analog, Xeloda, would be an effective therapy. Positive results from this pilot study would be used to extend the study to include a greater number of samples prior to consideration of a clinical therapeutic trial. A total of 40 samples will be examined in this pilot study.

### TECHNICAL APPROACH

Immunohistochemical analysis of archived tissue for TS, TP, and DPD.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Our results show that of 19 samples so far examined, approximately one-third of all thyroid cancers express favorable enzyme profiles (high levels of TP and low levels of DPD). This suggests that Xeloda might be an effective drug against some, but not all, thyroid cancers.

The number of subjects enrolled to the study since last APR at WRAMC is 19 and the total enrolled to date at WRAMC is 19. The total number enrolled study-wide is 19, if multi-site study.

### CONCLUSIONS

The data support the potential use of Xeloda in the treatment of thyroid cancer. The data have been presented in abstract form and submitted for consideration of publication. Further study may be required pending review of the manuscript.

## DETAIL SUMMARY SHEET

TITLE: In Situ Expression of *cagA* in *H.pylori* Infected Children - A Case Series with Endoscopic and Histologic Correlation

KEYWORDS: *Helicobacter pylori*, *cagA*, gastroduodenal disease, children, *in situ* hybridization

PRINCIPAL INVESTIGATOR: MAJ James R. Rick MC

ASSOCIATES: Dr. Andre Dubois, Dr. Cristina Semino-Mora, Dr. Eugenia Rueda-Pedraza, and Dr. Carolyn Sullivan

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Gastroenterology and Nutrition

INITIAL APPROVAL DATE: 10 July 2001

### STUDY OBJECTIVE

1. Describe the expression of *cagA* among *H.pylori* infected children using fluorescent *in situ* hybridization (FISH).
2. Describe the relation between *cagA* expression and gastroduodenal disease (endoscopic and histologic) in *H.pylori* infected children.
3. Describe the expression of MUC2 and MUC5AC among normal and *H.pylori* infected children using FISH and describe its relation to gastroduodenal disease.

### TECHNICAL APPROACH

Chart review and use of recuts made from archival gastric biopsies. These were subjected to Genta staining, immunocytochemistry, and FISH as described in the protocol. Data analysis is described in the protocol.

Chart review and slide recuts and staining complete.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No adverse events.

The number of subjects enrolled to the study since last APR at WRAMC is 51 and the total enrolled to date at WRAMC is 51. The total number enrolled study-wide is N.A., if multi-site study.

### CONCLUSIONS

The density of *H. pylori* colonization and *cagA* gene expression are increased with the severity of endoscopic appearance, the presence of intestinal metaplasia and with persistent infection. In addition, the proportion of *cagA*+ bacteria is increased in children with PUD, but not those with antral nodularity.

## DETAIL SUMMARY SHEET

TITLE: Open Label Administration of Human Botulism Immune Globulin

KEYWORDS: Infant Botulism

PRINCIPAL INVESTIGATOR: COL Harlan S. Patterson MC

ASSOCIATES: COL David I. Goldberg MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Critical Care

INITIAL APPROVAL DATE: 24 July 2001

### STUDY OBJECTIVE

Provide botulism immune globulin for victims of infant botulism.

### TECHNICAL APPROACH

Multi-center open label administration of botulism immune globulin. (Pending final FDA approval of product.)

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is *unavailable at time of submission*, if multi-site study.

### CONCLUSIONS

N/A

## DETAIL SUMMARY SHEET

TITLE: POG ALinC 17 – Induction Therapy for POG 9904, 9905, and 9906 (Consent Form Only)

KEYWORDS:

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC  
ASSOCIATES:

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 27 February 2001

### STUDY OBJECTIVE

This is the common induction regimen for the three POG ALinC 17 ALL studies.

### TECHNICAL APPROACH

Patients aged 1-21 years with newly diagnosed precursor B-cell ALL will receive this common induction therapy in an attempt to establish a remission prior to treatment on the appropriate low, standard, or high risk phase III therapeutic trial within the ALinC 17 protocols.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The three-drug induction on this protocol was temporarily closed on 27 November 2003 due to a high number of induction deaths. Whereas the induction death rates for other recent studies of similar risk ALL patients has been 0.3%-0.7%, the induction death rate on the P9900 three-drug induction was 1.3% (12 of 900). The P9900 remains open for "Classification Only", and "Four-Drug Induction". There have been no induction deaths at WRAMC, and all four patients enrolled on the ALinC protocols are post-induction and remain in remission on therapy.

### CONCLUSIONS

This study should stay open to support the ALinC 17 therapeutic trials.



## DETAIL SUMMARY SHEET

TITLE: POG 9904 - ALinC 17 Treatment for Patients with Low Risk Acute Lymphoblastic Leukemia:  
A Pediatric Oncology Group Phase III Study

KEYWORDS:

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC  
ASSOCIATES:

DEPARTMENT: Pediatrics  
SERVICE: Pediatric Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 17 April 2001

### STUDY OBJECTIVE

In patients with low risk precursor B-cell ALL: To compare short MTX infusion (regimens A and C) with a longer infusion (regimens B and D) with respect to efficacy and toxicity. To determine, in a randomized trial, if a delayed multi-drug intensification (regimens C and D) administered in the context of intensive anti-metabolite therapy will improve outcome for children with ALL. To determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction). To determine the relationship between a membrane bound glucocorticoid receptor and EFS via quantitation of the glucocorticoid receptor concentrations in marrow samples at diagnosis.

### TECHNICAL APPROACH

Patients ages 1 through 21 years with newly diagnosed low risk precursor B-cell ALL, after achieving remission with a standardized induction, are randomized to one of four regimens (A-D as above) with the following exceptions: (a) patients with trisomy 4/10 receive only A or B (regimens with no delayed intensification), while patients with the 1-19 translocation receive only C or D (regimens with delayed intensification).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

All subjects entering this protocol are entered on the P9900 classification and induction protocol. Since all three ALinC studies use the same induction regimen, the induction data are common to all three studies. The three-drug induction on the 9900 protocol was temporarily closed on 27 November 2003 due to a high number of induction deaths. There have been three deaths during the four-drug induction with prednisone (<1%). The P9900 remains open for "Classification Only" and "Four Drug Induction" while the protocol is being revised. There have been no post-induction deaths on the 9904. There have been no induction deaths at WRAMC and the patient enrolled on this protocol is post-induction and remains in remission on therapy. Toxicity, otherwise, has been within expectations, and is detailed in the reference cited below.

The number of subjects enrolled to the study since last APR at WRAMC is 1 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 483, if multi-site study.

[Ref: Children's Oncology Group Fall 2002 Meeting Report]

### CONCLUSIONS

Study should remain open.

## DETAIL SUMMARY SHEET

TITLE: POG 9905 - ALinC 17 Protocol for Patients with Standard Risk Acute Lymphoblastic Leukemia (ALL) – A Pediatric Oncology Group Phase III Study

KEYWORDS:

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC  
ASSOCIATES:

DEPARTMENT: Pediatrics  
SERVICE: Pediatric Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 27 February 2001

### STUDY OBJECTIVE

In patients with standard risk precursor B-cell ALL: To compare short MTX infusion (regimens A and C) with a longer infusion (regimens B and D) with respect to efficacy and toxicity. To determine in a randomized trial, if a delayed multi-drug intensification (regimens C and D), administered in the context of intensive anti-metabolite therapy, will improve outcome for children with ALL. To determine the correlation between event-free survival (EFS) and minimal residual disease (MRD)/early response. To analyze samples obtained at relapse to ascertain whether markers of MRD remain constant. To determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction). To determine the relationship between a membrane bound glucocorticoid receptor and EFS via quantitation of the glucocorticoid receptor concentrations in marrow samples at diagnosis.

### TECHNICAL APPROACH

Patients ages 1 through 21 years with newly diagnosed standard risk precursor B-cell ALL, after achieving remission with a standardized induction, are randomized to one of four regimens (A-D as above).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

All subjects entering this protocol are entered on the 9900 classification and induction protocol. Since all three ALinC 17 studies use the same induction regimen, the induction data are common to all three studies. The three-drug induction on the 9900 protocol was temporarily closed on 27 November 2003 due to a high number of induction deaths. The P9900 remains open for "Classification Only" and "Four Drug Induction" while the protocol is being revised. There has been a single post-induction death on the 9905. One child died in remission of Gram-negative sepsis during maintenance therapy. There have been no induction deaths at WRAMC, and the two patients enrolled on this protocol are post-induction and remain in remission on therapy. Toxicity, otherwise, has been within expectations and is detailed in the reference cited below.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 592, if multi-site study.  
[Ref: Children's Oncology Group Fall 2002 Meeting Report]

### CONCLUSIONS

Study should remain open.

## DETAIL SUMMARY SHEET

TITLE: POG 9906 - ALinC 17 Protocol for Patients with Newly Diagnosed High Risk Acute Lymphoblastic Leukemia (ALL) – Evaluation of the Augmented BFM Regimen - A Phase III Study

KEYWORDS:

PRINCIPAL INVESTIGATOR: Edwards, Glenn LTC MC  
ASSOCIATES:

DEPARTMENT: Pediatrics  
SERVICE: Pediatric Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 17 April 2001

### STUDY OBJECTIVE

To determine for patients at high risk for treatment failure if the augmented Berlin-Frankfurt-Muenster (BFM) therapy is superior to ALinC 14/15 therapy, on the basis of historical controls. To determine if minimal residual disease at the end of induction is predictive of an inferior prognosis. To determine the correlation between event-free survival (EFS) and minimal residual disease (MRD)/early response (ER). To determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction). To determine the relationship between a membrane bound glucocorticoid receptor and EFS via quantitation of the glucocorticoid receptor concentrations in marrow samples at diagnosis. To give POG investigators experience with BFM-type regimens as these will likely play a major role in COG protocols of the future.

### TECHNICAL APPROACH

Patients age 1 through 21 years are treated in a single arm study of the augmented BFM regimen in high risk acute lymphoblastic leukemia. The outcome for this regimen will be compared against historical POG regimens from ALinC14 and ALinC15. Historically, the four year event-free survival was 44% (S.E.=2.5%). This study is designed to have over 80% power to detect an improvement of 10% or more, at  $P < .05$ , one-sided, by Kaplan-Meier analysis.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

It is too early to report response or survival data. Induction toxicity, aside from early infection toxicity in the four-drug induction (see below), has been within expectations and is detailed in the reference cited below. All three ALinC 17 studies use the same induction regimen, but since subjects continuing on to this protocol receive only the 4-drug induction on the 9900, they are not affected by the problems associated with the 3-drug induction. There have been three deaths during the 4-drug induction with Prednisone (<1%) and 2 deaths during the 4-drug induction with dexamethasone (11%). In June 2000, the induction was amended to replace dexamethasone with prednisone in the 4-drug regimen because of toxicity. There have been no post induction deaths on this study. The WRAMC patient on this study is currently doing well post-induction in complete remission. The most common post-induction toxicity remains allergic reaction to asparaginase, occurring in approximately 40% of patients, and requiring a switch to PEG and/or Erwinia asparaginase. Two patients have been unable to complete all scheduled doses of asparaginase due to subsequent reactions to PEG and Erwinia asparaginase. Several CNS adverse events have been reported...none at WRAMC. Most have occurred during periods of IV methotrexate dose escalation (interim maintenance I and II) and have been rapidly reversible. The number of subjects enrolled to the study since last APR at WRAMC is 1 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 183, if multi-site study.

[Ref: Children's Oncology Group Fall 2002 Meeting Report]

CONCLUSIONS Study should remain open to accrual.

## DETAIL SUMMARY SHEET

TITLE: ANBL00B1: Neuroblastoma Biology Studies

KEYWORDS: Neuroblastoma; Biology; Risk Group

PRINCIPAL INVESTIGATOR: Edwards, E. Glenn LTC MC

ASSOCIATES: Mosijczuk, Askold COL MC; Reddoch, Shirley MD; Crouch, Gary LtCol MC; Merino, Margret MAJ MC

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Hematology-Oncology

INITIAL APPROVAL DATE: 24 April 2001

### STUDY OBJECTIVE

1. To prospectively analyze the factors currently used for risk-group assignment in neuroblastoma tumors at the time of diagnosis. 2. To maintain a reference bank containing clinically and genetically characterized tumor tissue and paired normal DNA obtained at the time of diagnosis (all patients), at the time of second-look surgery (high-risk patients), and relapse (all patients) for future research studies. 3. To prospectively analyze the prevalence of 1p, 11q, 14q LOH and gain of 17q; the expression of nerve growth factor and its high affinity (Trk-A) and low affinity (p75 NTR) receptors; and telomerase activity in neuroblastoma tumors compared to MYCN amplification, INSS stage, age, and histologic variables in predicting either response to treatment or outcome. 4. To build a database of the known biologic prognostic factors for patients on therapeutic studies.

### TECHNICAL APPROACH

Tumor tissue and blood from newly diagnosed neuroblastoma patients obtained at diagnosis and subsequent surgeries (relapse and second-look) are analyzed at reference laboratories for the factors listed above which are correlated with treatment response and outcome on COG neuroblastoma therapeutic studies. If available, neuroblastoma tissues, slides and nucleic acids are also stored for use in future studies. Enrollment on ANBL00B1 is a requirement for all neuroblastoma clinical trials open for patients at diagnosis. Banking of tissue is not a requirement for study registration.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study opened for patient registration on 5 January 2001. Enrollment on this study is a requirement for all neuroblastoma clinical trials open for patients at diagnosis. As of 24 February 2003, 1012 patients were registered on this study. Accrual is on target, and collection of diagnostic materials for clinical studies in the Neuroblastoma Reference Lab is proceeding smoothly. In addition, nucleic acids and tumor banking, as well as studies aimed at addressing Study Goal 3, are on track.

Unique to this protocol is rapid assessment of tumor specific variables (MYCN, DNA index, and Shimada pathology) necessary for risk group assignment. Only 2.7% of patients could not have a risk group assigned, typically due to an inadequate specimen submitted for analysis.

Since this is a non-therapeutic study, adverse event reporting is not applicable. A possible benefit to subjects is proper determination of risk factors to determine best treatment.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1, as opposed to 2, which was mistakenly reported in the last Annual Progress Report. The total number enrolled study-wide is 1012 as of 24 February 2003.

CONCLUSIONS Study should remain open.

## DETAIL SUMMARY SHEET

TITLE: Assessing States of Unconsciousness by Actigraphy

KEYWORDS: Actigraphy, Coma, Unconsciousness

PRINCIPAL INVESTIGATOR: LTC Michael Russo, MC

ASSOCIATES: COL Daniel Redmond, MC; COL Edward Urban, MC; LTC William Campbell, MC; LTC Kevin Cannard, MC LTC(P); Robert Labutta, MC; MAJ John Choi, MC; MAJ Al Martins, MC; MAJ Evan Murray, MC

DEPARTMENT: Neurology  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 20 March 2001

### STUDY OBJECTIVE

In the present study, states of unconsciousness will be explored using actigraphy. Actigraphy is already an accepted tool for distinguishing wake from sleep. Actigraphy will be compared to standard available measures for the assessment of unconsciousness in a hospital setting, specifically, the clinical neurological examination. Hypotheses that will be tested are:

- a. Actigraphic measures will reliably discriminate pathological unconscious states from normal sleep.
- b. Actigraphic measures will reliably distinguish various levels of unconsciousness.

### TECHNICAL APPROACH

This observational study will identify level of unconsciousness using the standard clinical examination. Four levels of unconsciousness will be assessed, with 12 samples collected from each level. This clinical exam data will be used to identify segments of actigraphic signal representing a specific level of unconsciousness. The actigraphic signal from each state of unconsciousness will then be examined for features that may distinguish a level of unconsciousness from other levels. The actigraphic signals will be compared using computational techniques including neural net analysis.

### PRIOR PROGRESS

Six volunteers signed consent. Of these six, one was not actigraphed and did not begin the study – the volunteer experienced an administrative scheduling conflict. Five volunteers enrolled. Data was collected from four volunteers. One volunteer who was actigraphed died during the study and the actigraph and data were lost. An adverse event report was filed; cause of death was unrelated to the protocol or the actigraph. The visual inspection of the data on the four subjects shows the actigraph device to be working according to design specifications. No medications were administered during the study. No patients voluntarily withdrew from the study.

The number of subjects enrolled to the study since last APR at WRAMC is 5 and the total enrolled to date at WRAMC is 5.

### CURRENT PROGRESS and REVIEW of RECENT LITERATURE

No new patients have been consented or enrolled since last APR. No new literature published on this topic.

### CONCLUSIONS

No conclusions can be made at this time.

## DETAIL SUMMARY SHEET

**TITLE:** Investigation of the Administration of Baclofen Injection for the Management of Spasticity Associated with Stroke, Medtronic Protocol #D98-072

**KEYWORDS:** Stroke, spasticity, Baclofen pump

**PRINCIPAL INVESTIGATOR:** Cannard, Kevin LTC MC  
**ASSOCIATES:** Choi, John MAJ MC; Moores, Leon LTC MC

**DEPARTMENT:** Neurology  
**SERVICE:**

**STATUS:** O  
**INITIAL APPROVAL DATE:** 27 March 2001

### STUDY OBJECTIVE

The primary objective is to evaluate functional changes as a result of Intrathecal Baclofen (ITB) therapy in the stroke population. Secondary objectives are to obtain additional data on the safety and efficacy of ITB therapy and to evaluate the quality of life changes as a result of ITB therapy.

### TECHNICAL APPROACH

In the first phase, at pre-screening, a medical history will be taken, and a medical examination will be performed. The patient will complete the Functional Independence measure (FIM) and Sickness Impact Profile questionnaires to assess function and quality of life, respectively. The patient will undergo manual muscle testing and have their spasticity evaluated with the Ashworth scale. At screening the patient must demonstrate a positive response to an intrathecal injection of 50 mcg, 75 or 100 mcg of baclofen. Spasticity will be assessed at 1,2,4,5 and 8 hours post-bolus injection. Heart rate, blood pressure and respiration will be assessed at each evaluation point of screening. A "positive response" is defined as an average one-point drop in the Ashworth score in the affected extremities as compared to the score obtained immediately prior to the bolus injection. This response must be maintained over two consecutive assessment points. IF the patient exhibits a significant reduction in spasticity, a SynchroMed Infusion System and catheter will be implanted to administer intrathecal baclofen on a chronic basis. In the second phase of the study, patients will return for office visits within 30 days and again at 90 days post-implant. Assessments (Ashworth Scale, review of current therapies) will be done a minimum of every 90 days (which is the maximum interval between pump refills of aclofen) until study termination. Dosage requirements, system function and side effects will be assessed at each follow-up visit. The patient will repeat the FIM and dSIP at 3 months and 12 months post-implant.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Summary of any recent literature has been provided to DCI. Study findings obtained thus far: None. (No new study findings were reported to us from Medtronic Company.) Amendments or modifications to the research study since the last review: None. Adverse events (AE) expected and/or serious for WRAMC site: None. Serious AEs for other sites: None. Information on patients withdrawn from the study at WRAMC: None. Information on patients withdrawn from the study at multiple centers: None.

The number of subjects enrolled to the study since last APR WRAMC is 0 the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is:

Active participating centers: 9  
Patients screened: 82  
Patients implanted: 63

Patients reaching 12-month follow-up: 43  
Patients discontinued due to death: 2  
Patients discontinued due to "other": 30

### CONCLUSIONS

No data was analyzed at this point and no new conclusions were drawn as informed by Medtronic.

## DETAIL SUMMARY SHEET

TITLE: Genes for X-linked Torsion Dystonia-Parkinsonism in the U.S. Veterans of Panay Filipinos

KEYWORDS: X-linked torsion dystonia-Parkinsonism, genetic mutation, movement disorder

PRINCIPAL INVESTIGATOR: COL Bahman Jabbari MC

ASSOCIATES: WenLiang Yan M.D. Ph.D. DSCCIP; Diarmuid Nicholson Ph.D., Yvonne Lukes DAC; Laura Pedraza DAC

DEPARTMENT: Neurology  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 15 May 2001

### STUDY OBJECTIVE

To identify the mutant gene, DYT3, causing X-linked Torsion Dystonia-Parkinsonism in the U.S. Veterans of Panay Filipinos.

### TECHNICAL APPROACH

Initial screen sample: A discordant brother trio with one affected brother and two unaffected ones are used. The blood samples of the two unaffected brothers, who are non-WRAMC beneficiaries, were collected through an approved protocol at the USUHS (RO92AL01).

Experimental approaches:

- a) The DNA and RNA extraction from the blood samples of the subjects is routine, with silica gel technology, following the manufacturer's instructions.
- b) B-lymphocytes from blood samples were transformed with Epstein-Barr-Virus to establish a cell culture to provide a source of mRNA for sequencing.
- c) Exon amplifications of the candidate gene are performed with regular PCR conditions together with at least 30-bp flanking splice donor or acceptor junctions. The PCR products are purified to remove primers before sequencing.
- d) Cycle sequencing is performed using BigDye dideoxynucleotide terminators (Applied Biosystems). To reduce cost the PCR primers used in the exon amplification are employed for sequencing.
- e) Mutation detection is conducted visually on the Sequencer program (Genecodes Software), comparing the sequence data from affected, unaffected and the public domain human DNA sequence (NCBI).

**PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE**

A 1.6 million base pair region of the X chromosome defined by the proximal marker DXS453 and the distal marker DXS559 has been divided into a proximal and a distal region. The two regions are approximately 450,00 base pairs in size separated by 725,000 base pairs. The distal region begins with marker, DXS10015 and ends with DXS559. It includes 11 possible genes. Genomic DNA sequence data was obtained from 5 of those genes, ITGB1BP2, LOC139125 (RhoG), STAT 4, FLJ23071 and CXCR3 (GPR9). Five polymorphic markers, which span the region, were also sequenced. The sequenced regions account for 4% of the total DNA. Two SNPs (single nucleotide polymorphism) were identified in non-coding regions. The first is in the intergene region between NONO and ITGB1BP2. The second is in an intron of the STAT 4 gene. All five polymorphic markers in the region are different for affected versus unaffected. Currently the proximal region defined by DXS 453 to DXS7113 is being sequenced. There are 13 possible genes in this region. LOC139562 does not have any sequence differences. LOC158833 has 4 exons and there are no sequence differences in the coding regions. There is a SNP in an intron when compared with the NCBI sequence; affected and unaffected have the same base. The gene P2RY4 has three base changes and they are in the coding region of this single exon gene. Two cause amino-acid changes and one is a silent change. In all three cases the affected patient and an unaffected brother have the same changes with respect to the NCBI sequence. DLG3 has been sequenced from genomic DNA and cDNA made from mRNA.

Alternate splice sites have been identified and there are exon segments that were not previously identified in the annotated NCBI sequence. However the alternate splicing is not restricted to the affected subject but is also seen in the unaffected siblings. A review article (Nemeth, A. H., 2002. Brain 125, 695-721) still locates the DYT3 gene in the Xq13.1 region. There are no adverse events to report.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 3, if multi-site study.

**CONCLUSIONS**

The region Xq13.1 is the critical region for the DYT3 locus and the analysis of genes in this region will continue. Careful study of the mRNA sequences may provide evidence for expression differences that are related to the disease.



## DETAIL SUMMARY SHEET

TITLE: Development of a Child and Adolescent Psychiatry Database

KEYWORDS:

PRINCIPAL INVESTIGATOR: Black, Nancy MAJ MC

ASSOCIATES:

DEPARTMENT: Psychiatry

STATUS: O

SERVICE: Child and Adolescent Psychiatry

INITIAL APPROVAL DATE: 17 October 2000

### STUDY OBJECTIVE

1. To gather comprehensive demographic and clinical data on consented clinic patients in order to categorize patients in terms of acuity, diagnoses and necessary treatments/interventions.
2. To create a database including clinic and telemedicine consultation patients to be utilized as a research vehicle for future retrospective and prospective studies of a military clinic population.

### TECHNICAL APPROACH

Parents/guardians of new clinic patients are approached in the child and adolescent psychiatry service (CAPS) clinic or via telemedicine sessions after completion of a standard intake paperwork packet. Consent for the study allows intake data from the clinic forms to be entered into a CAPS computerized database by the research assistant. There are no videotapes, blood draws, genetic testing, etc. performed for research purposes.

As of January 2002, CAPS switched the Ohio Scales outcomes measure. To maintain consistency within the CAPS computerized database, the research assistant has the parent/guardian complete the YOQ once they have been consented for the study.

### PRIOR AND CURRENT PROGRESS

There are no recent literature findings on child psychiatry databases. There are no study findings thus far; participants continue to be enrolled in the study. Since the last APR review, there was a change in the Principal Investigator, from Michelle Sandberg to MAJ Nancy Black. The study also underwent an audit review by the Department of Clinical Investigation in March 2002.

The number of subjects enrolled to the study since last APR at WRAMC is 32 and the total enrolled to date at WRAMC is 97.

There have been no adverse events.

### CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: Computer Automated Neurophysiological Assessment of Army Aviators

KEYWORDS: ANAM, CogScreen, Neuropsychology

PRINCIPAL INVESTIGATOR: Baggett, Mark MAJ MS

ASSOCIATES: Kelly, Mark P. and Christensen, Daniel

DEPARTMENT: Psychology

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 30 November 2000

### STUDY OBJECTIVE

Conduct a validation study comparing a computerized assessment measure Automated Neuropsychological Assessment Metric 2001 (ANAM2001) windows version (Bleiberg, Kane, Reeves, Garmoe, & Halper, submitted for publication) to CogScreen, SynWin and the Wonderlic Personnel Test (Wonderlic, 1983). The purpose of this study is to validate ANAM2001 as a future assessment tool when compared to CogScreen.

### TECHNICAL APPROACH

The design is a related measures construct-validity study (Bordens & Abbott, 1988; Campbell & Fiske, 1959; Glass & Hopkins, 1984) for one group of subjects. Specifically, the study will examine the convergent and discriminant validity, of the measures specified.

- a. Subjects: Subjects (125) will be U.S. Army Pilots assigned to the 160<sup>th</sup> Special Operations Aviation Regiment (SOAR) stationed at Ft. Campbell, KY. Subjects will be recruited via a flyer that is given to them when they in-process their unit. CPT John Via, the 160<sup>th</sup> SOAR Psychologist will be the Point of Contact for the study. The consent process will closely follow DOD Directive 3216.2. Any subjects who express an interest in this study will be given a copy of the consent form during scheduled recruitment sessions. Unit officers and senior NCOs in the chain of command shall not be present at the time of solicitation and consent. At all unit recruitment sessions, an ombudsman not connected in any way with the proposed research shall be present to monitor the voluntary nature of study participation. The ombudsman will also insure that the information provided about the research is adequate and accurate. Either CPT John Via or MAJ Mark Baggett will host recruitment sessions. All recruitment sessions will last 15 to 30 minutes and will include the presence of the ombudsman, Chaplain MAJ Austin assigned to FT. Campbell. He will observe recruitment sessions while in civilian attire. Potential subjects can sign the consent form at the time of the recruitment or up to two weeks after having attended a recruitment session. Subjects who decide to consent to the study after the two-week period will be required to attend another recruitment session prior to being accepted into the study. All subjects will be over the age of 18 years and male since there are only male pilots at the 160<sup>th</sup> SOAR. Pilots who have already completed their 160<sup>th</sup> SOAR initial training will not be included as subjects due to the operational demands of their mission. The study will be run for two years from its start date. There are no perceived risks with study participation.
- b. Inclusion and Exclusion Criteria:  
Inclusion:
  - 1) Subjects on initial training status phase at the 160<sup>th</sup> SOAR.
  - 2) Subjects will be asked if they would be willing to participate in this study.
  - 3) All subjects will be volunteers.
  - 4) No subjects will be required, coerced, directed or otherwise ordered to participate.

Exclusion:

- 1) Substance abuse history
- 2) Pre-existing psychiatric diagnosis
- 3) Neurological illness or injury
- 4) Recent concussion or history of moderately severe brain injury will be excluded.
- 5) Subjects who are acutely ill
- 6) Subjects receiving medication with the potential to alter cognitive functions

All pilots in the 160<sup>th</sup> SOAR are pre-screened on exclusion criteria 1, 2 and 3 prior to being accepted to the regiment by the regimental psychologist independent of this proposed study. Therefore, it is unlikely that any of the subjects will be excluded on these three criteria. Exclusion criteria 4, 5 and 6 may disqualify the pilots from being accepted into the study but would not necessarily disqualify them from continuing to be in the regiment.

- c. Study Design: The design is a related measures construct-validity study (Bordens & Abbott, 1988; Campbell & Fiske, 1959; Glass & Hopkins, 1984) for one group of subjects. Specifically, the study will examine the convergent and discriminant validity, of the measures specified.
- d. Methodology: Subjects will be asked to read and sign the consent form. The 160<sup>th</sup> SOAR Psychologist will conduct subject screening after the volunteers have implemented the consent form. Subjects will complete an online history questionnaire to determine medical, social and flight history. The background history questionnaire, ANAM, CogScreen and SynWin will be administered by computer in a secure environment within a single 2-hour session. Testing of subjects will be conducted in a computer room at the 160<sup>th</sup> SOAR and observed by a Clinical Psychologist in groups of 6. The sequence of administration of the three tests (ANAM, SynWin and CogScreen) will be randomized to control for fatigue effects. The background questionnaire, ANAM and SynWin will be web enabled for this study. The background questionnaire and tests will be administered from a password protected web page on a secure server maintained at WRAMC, by WRAMC Telemedicine. The study will be conducted from computers at the 160<sup>th</sup> SOAR in a secure room. If it is technically feasible the CogScreen will be web-enabled. If this is not possible due to the commercial nature of the test, CogScreen will then be loaded to the local computers at the 160<sup>th</sup> SOAR. The data will up-loaded in SQL-7 from the 160<sup>th</sup> SOAR computers to a secure, password-protected server at WRAMC. The data will be saved into SPSS for later data analysis. All computers used in administration of the testing will be kept in a secure room at the 160<sup>th</sup> SOAR, which is locked when not in use. Access to the data on the computer will be gained only through passwords. All tests will include only a code number beginning with code "001." No name or social security number will be attached to the SPSS data files. Five years following the completion of the study all data files related to the study will be destroyed. Participation will be completely voluntary with the goal of enhancing US Army Aviation through developing cognitive performance screening measures (see attached consent form). Because of limited population size of the 160<sup>th</sup> SOAR it will not be feasible to randomly sample subjects from the population. A clinical psychologist at Ft. Campbell, KY will screen all test subjects utilizing structured clinical interview and questionnaires. The Wonderlic Personnel Test (WPT) is routinely included in the 160<sup>th</sup> SOAR screening process as a requirement of entry into the regiment. The WPT is administered independent of this proposed study. The WPT is a brief group administered test that correlates highly with IQ and is widely used in personnel settings (Wonderlic, 1983). The test is administered in order to predict academic performance of pilots on flight training materials. The WPT is thought to have little relationship with actual flight performance. The WPT is part of a standard screening battery that is given to all soldiers assigned to the 160<sup>th</sup> SOAR. The scores from the WPT will be available for data comparison with their consent. To control for potential effects of fatigue, subjects will be tested in the morning following a routine night's rest.
- e. Data Collection: A brief demographic questionnaire will be administered prior to beginning the testing (see appendix A). The questionnaire requires approximately 2 minutes to fill out. The purpose of the questionnaire is to collect medical history and demographic data that may be utilized to anonymously describe group data in any future publications. The questionnaire will not include name, social security number or other identifying information. Each subject will be assigned a code for their data e.g. "001" that

- f. will match the subjects questionnaire and tests to the same subject. A traditional measure of intellectual abilities the WPT will be used as a comparison measure of discriminant validity. The WPT is a paper and pencil self-administered test that takes 12 minutes to complete. The WPT correlates .91 to .93 with the Wechsler Adult Intelligence Scale (WAIS) Full Scale IQ (Wonderlic, 1983) a measure of general intellectual ability. Unlike ANAM, CogScreen, and SynWin the WPT tasks focus on accuracy of solving a variety of problems. Extensive research has been published with the WPT in personnel assessment and selections settings. Three computerized neuropsychological measures will be administered ANAM, CogScreen and SynWin. Data from each of three computerized neuropsychological measures is collected at the time of administration. The specific data that we are planning to analyze is shown on the attached data collection sheet. All measures are described in detail below.

There have been no modifications.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no published research papers that would add to the information already contained in our literature review.

The number of subjects enrolled to the study since last APR at WRAMC is 16 and the total enrolled to date at WRAMC is 36. The total number enrolled study-wide is 36 if multi-site study.

#### CONCLUSIONS

No conclusions have been made at this time.

## DETAIL SUMMARY SHEET

TITLE: CD-ROM Technology to Increase Appropriate Self-Care and Preventive Behaviors Among Enlisted Women

KEYWORDS:

PRINCIPAL INVESTIGATOR: James, Larry C. LTC MC  
ASSOCIATES:

DEPARTMENT: Psychology  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 5 June 2001

### STUDY OBJECTIVE

Determine if CD-ROM technology can increase preventive health knowledge in enlisted women.

### TECHNICAL APPROACH

CD-Rom technology. No modification to the study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The PI was deployed from December 2002 to May 2003. He began training evolutions for the deployment in October of 2002, and thus not much activity has occurred with the study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 6. The total number enrolled study-wide is 6, if multi-site study.

### CONCLUSIONS

We will make every attempt to complete the study as it was approved.

## DETAIL SUMMARY SHEET

TITLE: Army Nurse Readiness

KEYWORDS: Nursing, deployment

PRINCIPAL INVESTIGATOR: MAJ Peter H. Murdock AN

DEPARTMENT: Nursing  
SERVICE:

STATUS: C  
INITIAL APPROVAL DATE: 2 January 2001

### STUDY OBJECTIVE

1. To further assess the psychometric properties of the Readiness Estimate and Deployability Index (READI) in a large, diverse population of Army Nurses, and to make recommendations for the revision of the READI based on the results of this research.
2. To compare the results of this administration of the READI between active and reserve component Army Nurses in the North Atlantic regional Medical Command.

### TECHNICAL APPROACH

Data collection was conducted using a modified three-mailing procedure per the original protocol. The initial mailing began on 19 March 2001. Surveys were accepted through 19 July 2001 per protocol procedures. All participation was voluntary confidential.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There were no adverse events associated with this study. No new surveys were accepted since the last APR. The total number of subjects enrolled in the study is 324.

#### Literature review

Since December 2000, the work by Kovats and colleagues on the READI cited in the literature review in this protocol has been presented in several conferences. A Graduate Management Project on partial results of this administration of the READI (n=188 active and n=56 reserve nurses) was submitted and accepted in partial fulfillment of the requirements for the Master's Degree in Health Care Administration from Baylor University in May 2001. A recent literature review found no new articles related to operational assessment of nursing deployment readiness.

#### Study Results

Once the study was underway it became increasingly difficult to get accurate names and addresses for the majority of reserve nurses in the estimated population (n=1000) due to the reserve transition into AC/RC integration units. Lack of accurate contact data, time constraints related to completing the Graduate Management Project by May 2001, and the 120 day window for accepting surveys required the PI to suspend efforts to contact AC/RC units and target reserve nurses who are assigned to troop program units that deploy to an MTF in the NARMC (n=320). Surveys were sent to active component nurses and reserve nurses assigned to troop program units that deploy to an MTF in the NARMC. The inability to contact large numbers of reserve nurses contributed to a smaller combined sample size and may have contributed to the insubstantial results of exploratory multivariate principal component analysis.

#### Return Rate

Surveys were accepted up to 120 days after the initial mailing on 19 March 2001. The random sampling and modified three-mailing procedure used in this study achieved a 51% response rate (n=219) among the 425 active component nurses surveyed out to the NARMC active Army Nurse population (n=536), resulting in precision (e) for generalizability of  $\pm 5\%$ . There was a 42% response rate (n=105) among the 250 reserve component Army

Nurses surveyed in the population of nurses in troop program units that deploy to an MTF in the NARMC (n=320) resulting in precision (e) for generalizability between  $\pm 7\%$  -  $\pm 10\%$ . Overall return rate of 48% achieved a combined sample size of n=324.

#### Data Analysis

The READI was successfully used to describe and compare the nursing deployment readiness status of the two groups. Results were depicted in graphic operational format using the 1-5 scale augmented with the “Red-Amber-Green” zones for easy comparison. Generally the scores for both groups followed the same “pattern” of readiness and remained in the amber to green range with the exception of some of the knowledge-based questions in the operational nursing section that were in the red zone. Group item mean scores were compared for differences in overall readiness and dimensional readiness by section using a two-sample t-test. There was no significant difference found in overall readiness between the groups. The active duty group reported significantly higher mean scores for survival skills ( $t = 2.49$ ,  $p < .05$ ) than the reserve group. Between-group differences in item mean scores for the other sections of the READI were insignificant. Coefficient Alpha Reliability estimates of scaled READI items were consistent with previous reliability estimates in each section (.70 - .96) and in the instrument overall (.92). These results support the previous research findings that the READI is a reliable instrument for assessing the basics of nursing readiness. The results of exploratory multivariate principal component analysis did not support Reineck’s hypothesized six dimensions of readiness. The factor structure from this administration revealed 23 dimensional components with Eigenvalues >1 accounting for 69% of the solution. One component accounted for 18.5% of the solution and components 1-6 accounted for 42% with Eigenvalues 2.57 or greater.

#### CONCLUSIONS

This was the first successful mass-mail administration of the READI to active duty and reserve component nurses affiliated with a single Army regional medical command and achieved the largest combined sample of any previous administration (n = 324). The strengths of this study were its approval by the WRAMC IRB, the random selection of nurses, high response rate by active component nurses using the modified three-mailing procedure, and its emphasis on maintaining subject voluntariness and confidentiality. The greatest research challenge in completing the study was getting accurate contact data from the reserve component. The READI can improve nurse deployment readiness in a variety of ways. Groups of nurses from different sections, units, or regions can be compared and their readiness ratings matched with mission-specific casualty care projections to find the best fit between mission requirements and nursing personnel. Individual nurses can be evaluated for suitability for specific missions when small forward-deployed teams are being created to respond to worldwide crisis contingencies. New nurses assigned to PROFIS positions, field or reserve units can be assessed for their readiness level and training needs when they arrive in a unit compared with their other unit cohorts and reassessed over time against unit, regional, and MEDCOM-wide READI benchmark ratings. Over time, commanders, nurse leaders, unit historians and others can plot changes in readiness as the history of unit training exercises and deployments unfolds. Data from multiple READI administrations can be used to build a profile of Army Nurse skills that can aid in recruitment and ensure that elected officials and policy makers are aware of the value of Army Nurses in contributing to a responsive, competent ready Army medical force. The instrument needs preparation for electronic format, and institutionalization in the readiness reporting system. Arrangements for adaptation to the U.S. Air Force and further testing of the instrument are being made with a doctoral student in long-term health education and training at The University of Maryland at Baltimore. With development of a self-scoring guide and dissemination in several media formats, the READI has great promise to provide a richer, more comprehensive estimate of readiness and deployability among military health care personnel in today's exceptionally high operational environment.

## DETAIL SUMMARY SHEET

TITLE: Improving Adherence in a Coronary Disease Reversal Program with Web-Based Technology

KEYWORDS: Cardiovascular disease prevention; outcomes assessment; web-based technology; adherence

PRINCIPAL INVESTIGATOR: Patrician, Patricia A. LTC AN

ASSOCIATES: Walizer, Elaine LTC (ret) AN; Vernalis, Marina COL MC

DEPARTMENT: Nursing

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 20 February 2001

### STUDY OBJECTIVE

The overall purpose of this study is to conduct a randomized comparative study to measure the efficacy of an Internet-based interactive communication link as an aid to promote patient adherence to a coronary artery disease reversal program. The study seeks to answer the research question: "What is the overall effect of an internet-based interactive communication link on the efficacy of a lifestyle modification program?" The study will address four research aims.

1. To determine if the use of an Internet-based interactive communication link (Health Hero Network® Online Services) between participants enrolled in the Coronary Artery Disease Reversal (CADRe) program and CADRe clinical team produces a significant change in program adherence.
2. To determine if the use of an Internet-based interactive communication link (Health Hero Network® Online Services) reduces the patient's cardiac risk factors as a result of adherence to the program.  
Sub question: To determine the feasibility of using comorbid disease specific questions via the communication link to initiate a more rapid intervention if needed.
3. To determine the patient satisfaction level with use of this technology as an adjunct intervention to the CADRe program.  
Sub question: To determine if there is an association between the total adherence score at program exit and overall patient satisfaction with the technology.

### TECHNICAL APPROACH

A randomized comparative design will be used to determine the efficacy of an Internet-based interactive communication link (Health Hero Network® Online Services) in the adherence to a coronary artery disease reversal program. Participants will follow a controlled protocol and receive either Health Hero Network® Online Service plus standard Program or the standard Program based on randomization of the cohort upon entering the Program. In this study, the groups that do not receive the Health Buddy® will be considered the control group. Participants will be recruited from the Cardiology Service and the "Non-Invasive Coronary Artery Disease Reversal" study. Cohorts of up to 20 patients are recruited every three months for enrollment. Cohorts of patients will be randomly selected (using a random number table) to receive the Health Buddy® Appliance. Irrelevant of cohort size, at least two cohorts will use the Health Buddy® Appliance to minimize one cohort being seen as "special". The goal is 60 patients who use the Health Buddy® appliance and 60 controls. This will allow for those who choose not to participate and for dropouts. Selection for this study will be done by random pre-selection of cohorts as a whole prior to recruitment into this study. Cohorts will be randomized to the Health Buddy® group or standard Program care using a table of random numbers. If the cohort is randomized to the Health Buddy® group, participants not willing to use the Health Buddy® appliance will be offered the opportunity to decline its use and dropped from this study (not the host study); however, demographic data will be collected on those who choose not to participate. This demographic data is already collected in the host study and will be maintained in the host study research records. Those declining use of the Health Buddy® will remain with their cohort and receive standard Program care. Patients in the randomized Health Buddy® group who do not wish to use the device will not be removed from the cohort, but their data will not be used as control data. Only those patients randomized to the treatment group will be consented



for this study.

The WRAMC Human Use Committee (HUC) approved this protocol on 20 February 2001 and required revisions were received on 29 March 2001. Subsequent USUHS IRB approval was received on 13 June 2001.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

##### Study Addenda

No study addenda since last annual progress report.

##### Enrollment

The number of subjects enrolled to the study since last APR at WRAMC is 35 (treatment group) and 24 (control group) and the total enrolled to date at WRAMC is 79. Please note that only the treatment group is consented for this study. The control group subjects are those enrolled in the study protocol WU# 1229-99. Of the treatment group participants, 23 are receiving the study treatment, 14 have withdrawn, and 18 have completed the study. Additionally, two subjects that originally consented to use the treatment device decided against its use prior to starting the study program. One of these subjects has since withdrawn from the core protocol and is included in the withdrawal statistics. These data will not be used as part of the control group. In the control group, 10 are receiving the core study treatment, 2 have withdrawn, and 12 have completed the one-year study. The above withdrawals are not a direct result of this study's treatment, but have withdrawn from the core study. Enrollment for control subjects should be completed in April 2003.

##### Adverse Events

There have been no adverse events as a result of this study.

##### Preliminary Data

Table1: Summary of Demographic Statistics

Factor	Sample Mean	Sample Range	Rx Grp Mean	Control Grp Mean	Sample Std.
Age	58.2	31- 79	58.3	58.1	10.0
Yrs. of Education	17.5	12-28	17.4	17.8	2.7
Weight	201.6	97-377	200.6	203.9	53.4
BMI	29.9	18-50	29.6	30.7	6.2

Table 2: Gender, Military Status & Cardiovascular History

Factor	Sample Freq/%	Rx Grp Freq/%	Control Grp Freq/%
Male	52 / 66%	39 / 71%	13 / 54%
Female	27 / 34%	16 / 29%	11 / 46%
Military Status			
AD	18 / 23%	11 / 20%	7 / 29%
Ret	43 / 54%	31 / 56%	12 / 50%
Dependent	17 / 22%	12 / 22%	5 / 21%
Other	1 / 1%	1 / 2%	0
Evidence of CAD	42 / 53%	32 / 58%	10 / 42%
Revascularization	35 / 44%	28 / 51%	7 / 29%
Statin therapy use	53 / 67%	36 / 66%	17 / 71%
Diabetes	10 / 13%	6 / 11%	4 / 17%
Hypertension	42 / 53%	28 / 51%	14 / 58%

Preliminary comparisons between the treatment group and control group cannot be made at this time due to small sample size in the control group (n=12). Adherence data via personal adherence logs and Health Buddy® data export have not yet been fully analyzed, but represented below is preliminary adherence data for the three-month

time point for the one control group (n=12) and two of the treatment group cohorts. Data for specific cardiovascular risk factors (i.e. lipids, other serum markers, BP, weight) has not yet been analyzed for this report.

Table 3: Program Component Adherence at 3-months

Factor	Rx Grp Mean	Control Grp Mean
Overall Diet (%)	86%	92.7%
Stress Management (%)	74.6%	71.7%
Aerobic Exercise (%)	103%	80%

The Health Buddy® Satisfaction survey has been completed on 19 participants enrolled in the treatment group that have either completed the study or have withdrawn. Participants were generally very satisfied or satisfied with the Health Buddy® device (79%); 69% felt use of the device encouraged their overall adherence to the program components, and 63% stated the device helped them stay motivated with the program.

### CONCLUSIONS

No objective conclusions can be made at this point in time due to the small control group sample size. Patient approval with the device seems high after some initial frustration with data entry using the electronic device. Observationally, it appears that high-risk symptoms management improved (i.e. chest pain and blood glucose) as well as fewer high-risk behaviors (i.e. compliance with overall program components) being reported by the subjects.

## DETAIL SUMMARY SHEET

TITLE: Medication Error Reporting and the Work Environment in a Military Setting

KEYWORDS: medication errors, patient safety, work environment

PRINCIPAL INVESTIGATOR: LTC Patricia Patrician, AN

ASSOCIATES: COL Laura R. Brosch, AN

DEPARTMENT: Nursing

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 10 July 2001

### STUDY OBJECTIVES:

- 1) Assess the differences in medication error reporting between an anonymous report and the current formal incident report system. Only those errors that occur on inpatient wards will be considered.
- 2) Assess civilian and military nurses' perceptions of the nursing work environment, reasons for medication errors, reasons for non-report and extent of non-report.
- 3) Examine the relationship of the nursing work environment (unit-based and shift-specific factors) and medication error reporting in an Army Medical Treatment Facility (MTF).

TECHNICAL APPROACH: This study consists of a cross-sectional anonymous survey and anonymous longitudinal daily coupons completed by nurses over a 30-day period. We plan to resume data collection in mid-June 2002.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE:

There have been no adverse incidents concerning this study. We have completed data collection on all wards and are in the final stages of data analysis. While the literature on medication errors addresses the causes and consequences of medication errors and efforts to reduce their occurrence, no new literature has been published dealing with reasons for not reporting medication errors. MEDCOM has recently conducted a patient safety organizational climate survey and results show that a "culture of blame" for errors in health care (not only medication errors) still exists within the Army health care system, although this information has not yet been published.

### RESULTS

**Response Rates:** The sample included RNs and LPNs who worked at least two days per week on that ward. Fourteen inpatient units in one military academic military center were included in the study. The response rates for the cross-sectional survey were 16%. Of the 268 surveys that were distributed, only 43 were returned. The response rate by ward was 0% to 45%. An interesting observation is that the ward that normally turns in the most formal incident reports each month had the highest response rate. The response rates for the longitudinal coupons by ward were 3.5% to 26%, with an overall response rate of 11%. Potential participants worked a total of 4125 "person-shifts" during the study period; 462 coupons were returned.

**Sample characteristics:** Because of the sensitivity of the topic under study, the researchers purposely did not include many demographic variables. The mean nursing experience of those responding to the cross-sectional survey was 11.6 (SD 11) years. The mean unit tenure of the nurses was 4.88 (SD 7.85) years. Because floating to other wards and rotating shifts are indicative of personnel turbulence and are viewed as unpleasant in other nursing studies, the research team asked participants to indicate the frequency with which they floated or rotated shifts within the past two weeks. Surprisingly, the majority (80%) stated they did not float to another unit within the past two weeks. Four people (10%) indicated they floated once and four (10%) indicated they floated more than twice during the past two weeks. In terms of rotating shifts, the majority (51%) indicated that they did not rotate shifts during the past

two weeks; twelve (29%) indicated they had rotated shifts once; four indicated (10%) “twice”, and four (10%) indicated “more than twice”.

Reasons for medication errors: One section of the cross-sectional survey asked about reasons why medication errors occur on that ward. The nurses were asked to rate these reasons on a six point Likert scale as they agree. The midpoint, a score of 3.5, was used as a cut-off score. That is, anything above a 3.5 was a reason for medication errors; scores below 3.5 were not reasons for medication errors. Figure 1 shows the reported reasons why medication errors occur. The top reason was that orders change frequently.

Percent of medication errors reported: Participants were asked to report the percentage of medication errors that are reported on their ward. Choice ranges were broken down by 10-percent increments, i.e. 0-10%, 11-20%, and so forth. The categories were further collapsed into 20% increments. As Table 1 depicts, the majority (38%) of responses were in the 0-20% category, and 28.5% of the responses were in the 21-40% category. Taken together, 66.6% of the respondents indicated that less than 40% of all errors that occur on their wards are formally reported.

Figure 1. Reasons for Medication Errors

Doctor's orders change frequently	4.6%
Interruptions while passing meds	4.53%
Not enough in-services on new drugs	4.28%
Names of meds similar	4.02%
Pharmacy delivers incorrect dose	3.86%
Doctor's note not clear	3.84%
Patients on similar meds	3.77%
No communication when next dose due	3.7%
Look-alike meds	3.7%
Look-alike packaging	3.6%

Things that were not issues were: legibility of doctor's orders, nurses not adhering to proper med procedure, limited knowledge about meds, pharmacy availability, abbreviations, knowledge of allergies, equipment malfunctions, and inability to pass all meds in allotted time frame.

Table 1. Percent of Medication Errors Reported on Your Unit: Self-Report

Response Category	N	%
0-20%	16	38.1
21-40%	12	28.5
41-60%	4	9.6
61-80%	5	11.7
81-100%	5	11.9

Another objective of this study was to compare the number of formally reported medication errors to those reported on the anonymous coupons. As shown in Table 2, during the same dates of the study, 108 anonymous error reports were received, and 14 formal incident reports were received at that same time. When the research team compared the dates and approximate times of the errors, only six were duplicates, meaning they were reported both formally and for this study. This indicates a 5.6% error-reporting rate. Near misses were reported at a rate of 15%.

Table 2. Formal versus Anonymous Reporting: Actual Reports

	Formal Incident Reports	Anonymous Reports	Matched Reports (Anonymous + Formal) Reporting Rates in Parentheses
Error	14	108	6 (5.6%)
Near Miss	10	40	6 (15%)
Totals	24	148	12 (8%)

Another objective of this study was to determine reasons why nurses don't report medication errors. This scale was structured similarly to the Reasons for Medication Errors scale in that it had a six-point Likert scale, with 1=strong disagree and 6=strongly agree. Figure 2. shows the results of this scale. The strongest reason given for not reporting errors is that the administration looks at individuals, not systems. Other reasons are shown in the graph.

**Figure 2. Reasons for Not Reporting Medication Errors**

Administration looks at individuals, not system	4.84%
Nurses are blamed if something happens to patient due to error	4.6%
Nurses fear adverse consequences from reporting	4.51%
Nurses believe peers will think them incompetent	4.44%
Nurses do not think error is important enough	4.12%
Patient/family may sue	4.12%
No positive feedback when meds given correctly	4.07%
Nurses afraid of reprimand from physician	3.77%
Response from administration does not match the severity	3.67%
Report takes too long to complete	3.65%

The things that were not problematic include: Agreement about definition of error, recognition of error, and contacting the MD taking too long. From these items, subscales were constructed to summarize the data. The subscales, validated in previous work by Wakefield and colleagues, were: Fear, Administrative Response, Disagreement over Error, and Reporting Effort. The highest scores were: Fear (mean 4.29, SD 1.33) and Administrative Response (mean 4.04, SD 1.02). Nurses scored lower on Disagreement over Error (mean 3.32, SD 1.09) and Reporting Effort (mean 3.06, SD 1.16), indicating these were not reasons why medication errors were not reported. Finally, the work environment was assessed using the Nursing Work Index, Revised (NWI-R). The subscales of interest in this instrument were Nurse-Physician Collaboration, Autonomy, Control Over Nursing Practice, and an overall Composite Index. Table 3 depicts these results.

**Table 3. NWI-R Subscale Scores**

Subscale	Items	Alpha	Mean (SD)
Administrative Support	5	.89	2.73 (.79)
Resource Adequacy	4	.73	2.71 (.61)
Nurse-Physician Collaboration	3	.83	2.81 (.69)
Composite Index	21	.94	2.65 (.49)

Items in the NWI-R are graded along a four-point Likert scale with 1=strongly disagree and 4=strongly agree. Therefore, a higher score indicates a more favorable work environment. Table 3 shows that of the subscales, nurses rated their collaboration with physician colleagues as most favorable.

## **CONCLUSIONS**

There are very specific reasons for the occurrence of medication errors according to the nurses who responded to the cross-sectional survey. These reasons need further investigation. For example, one wonders why medication orders change so frequently, how interruptions can be minimized while passing medications, and what can be done about look-alike and sound-alike medications. We need to work towards a better system for medication delivery to reduce missing doses and delays. Finally, we, as an organization, have a long way to go before the culture changes to one of non-retribution. This study provided actionable information to address the error rates associated with medication administration. In addition, it shed light on reasons why nurses at this organization are reluctant to report medication errors. The research team is not completely finished with the data analysis and will send in a final report in the future.

## DETAIL SUMMARY SHEET

TITLE: Research Utilization of Registered Nurses in U.S. Army Hospitals

KEYWORDS: Research Utilization, Research Based-Practice

PRINCIPAL INVESTIGATOR: LTC Laura Brosch, AN

DEPARTMENT: Nursing

STATUS: C

SERVICE:

INITIAL APPROVAL DATE: 20 July 2001

STUDY OBJECTIVE

To determine the extent that nurse in US Army MTFs use research findings for their own practice, to describe the ways in which research findings are used among different levels of nurses, and to describe both professional and organizational factors that enhance or hinder research utilization.

TECHNICAL APPROACH

Participants at three sites [Walter Reed Army Medical Center (WRAMC), Womack Army Medical Center (WAMC), and Ireland Army Community Hospital (IACH)] were asked to complete two survey instruments. One assessed research utilization and professional factors that may affect it. The other identified organizational factors that may impact implementation of research findings in practice. IACH was used as a pilot site to corroborate reliability and validity of these instruments for use with this population. A personal visit to each chief nurse was made to discuss questions and concerns regarding the study. The investigator requested a name only list of all RNs working at each facility. This was used expressly for the purposes of personalizing the first mailing of the survey and providing a directed second mailing and reminder letters if necessary. At the time of study commencement, a reminder explanatory letter was sent to the Chief, Department of Nursing, at each of the facilities. The study aims, purpose, and procedures were discussed, as well as time frames for the study, IRB approval, and compliance. Packets sent to all the nurses in each facility included a cover letter providing details of the study, iterating that participation was voluntary, and that confidentiality of responses would be strictly maintained. It also included the two survey instruments and a postage-paid return-mailing envelope. Voluntary return of the surveys to the associate investigator constituted consent to participate in the study. Survey mailings to the pilot site (IACH) commenced on 5 November 2001 following an announcement letter to the Chief Nurse and flyer distribution. Data collection proceeded according to the stated protocol, and ended on 17 December 2001. Survey mailings for WAMC began on 7 January 2002 with a letter to the chief nurse and flyers. Surveys were mailed out beginning 21 January 2002. Final thank you letters were sent on 11 March 2002. Survey mailings to WRAMC began on 27 February 2002 following a prior announcement letter to the chief nurse and flyer distribution. Final thank you letters were sent on 27 March 2002. Table 1 outlines the numbers and percentages of surveys returned from each site and the usable ones entered into the database.

	Site A Community Hospital	Site B Large Medical Center	Site C Small Medical Center	Total
Population				
Military	35	272	112	419
Civilian	53	234	154	441
	88	506	266	860
Sample				
Military	18 (51.4%)	108 (39.7%)	39 (34.8%)	164 (39.1%)
Civilian	20 (37.7%)	83 (35.5%)	45 (29.2%)	148 (33.6%)
	38 (43.2%)	191 (37.7%)	84 (31.6%)	313 (36.4%)
Usable Surveys				
Military	18 (51.4%)	105 (38.6%)	37 (33.0%)	160 (38.2%)
Civilian	17 (32.1%)	71 (30.3%)	42 (27.3%)	130 (29.5%)
	35 (39.8%)	176(34.7)	79 (29.7)	290 (33.7%)

**PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE**

Newer literature in this area of study is moving away from the individual problems in implementing evidence into practice and toward focus on the organization as a system of change. Interactions of the professional and organizational factors with the environment are beginning to surface as significant to the process of research utilization. In addition, the term “research utilization” has evolved to “evidence-based practice”, “knowledge utilization”, and most recently, “knowledge transfer”. These new terms are broader and recognize that research is not the only source of knowledge for best practice.

A total of 313 of 860 surveys were returned from the three study sites, for a return rate of 36.4%. Of those, 23 were not included in the database for various reasons including large amounts (>25%) of missing data. The total number of usable surveys was 290. Because this study consisted only of surveys and participation was voluntary, it is assumed that there have been no adverse events associated with it at any of the three sites. None have been reported.

The number of subjects enrolled to the study since last APR at WRAMC is 3 and the total enrolled to date at WRAMC is 191, with 176 usable. The total number enrolled study-wide is 313, with 290 usable.

**CONCLUSIONS**

Data analysis for this study supported the past literature in perceived barriers to research utilization. Lack of organizational support, willingness to suspend current beliefs to change practice, attitudes toward research, and access to evidential knowledge was considered barriers to implementation in this sample. It has always been assumed that educational level was directly related to increased use of research in practice. Yet, in this study, the mean educational level was lower. When environment was added as a variable and a regression model applied to analyze these groups, there was no difference in overall research utilization scores. However, there were differences between the groups in terms of interaction between environment as a variable and the factors of belief suspension, and attitudes toward research and access to research findings. Further, research is warranted in this area to determine the nature of the interactions and how they cause nurses either to use, or not to use, evidence in their practice.

## DETAIL SUMMARY SHEET

TITLE: Army Hospitals - Work Environment, Quality of Care, and Intent to Leave

KEYWORDS: Hospital nursing, work environment, retention, quality of care

PRINCIPAL INVESTIGATOR: LTC Patricia A. Patrician, AN

ASSOCIATES: LTC Laura R. Brosch, AN; COL Melissa Forsythe, AN

DEPARTMENT: Nursing

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 10 July 2001

### STUDY OBJECTIVES

- 1) Describe work environment attributes, affective responses to the job (burnout and job satisfaction), perceived quality of care, and intent to leave the Army workforce from the perspective of military and civilian staff nurses working in Army hospitals,
- 2) Explain the relative contributions of individual attributes, work environment attributes, and affective responses to the job in explaining intent to leave the Army workforce, and
- 3) Examine the added contribution of nurses' perceptions of the quality of care they provide in explaining intent to leave the Army workforce.

### TECHNICAL APPROACH

29 May 2002 to 1 June 2003: Described in TriService Nursing Research Program (TSNRP) Progress Report.

10 July 2001 to 28 May 2002: This is a multi-site, cross-sectional study of nurses who work in inpatient units in the Army Medical Department. The plan for this study was to obtain lists of units and names of the nurses who work there from each medical treatment facility (MTF). We then planned to conduct surveys in accordance with the Dillman method of survey methodology. However, at least one site (MAMC) objects to releasing the names of their nurses to the research team and prefers to generate the list of names and codes locally and distribute the surveys to each nurses' mailbox. This would further protect against any inadvertent breaches of confidentiality as we would not have access to those nurses' names at all. We would receive the surveys by mail at WRAMC and provide MAMC the codes of the returned surveys. They would then track responses and re-send surveys to those who did not respond to the first mailing.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

29 May 2002 to 1 June 2003: The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total enrolled at NARMC is 99. The total number enrolled study-wide is 1511, if multi-site study. The last two MTFs will be surveyed this summer and fall.

Since the last APR, all the IRBs have been approved except for William Beaumont Army Medical Center (BAMC). We have been given verbal IRB approval, but we are awaiting formal notification. All the MTFs identified to participate in the study have been surveyed at least once except for WRAMC and WBAMC. Because nurses at WRAMC have received too many surveys during this fiscal year, we are waiting until June 2003 to survey WRAMC. WBAMC will be surveyed as soon as we receive IRB approval from WBAMC's IRB and secondary approval from USUHS's IRB.

First survey distribution at Moncrief Army Community Center (MACH) and Tripler Army Medical Center (TAMC) did not occur according to the original plan for data collection. Each Deputy Commander for Nursing chose the option to have a local Point of Contact (POC) distribute the surveys. The POC at MACH had the Head Nurses of each inpatient unit maintained the spreadsheets. When the Head Nurses deployed, the local POC did not have access to their spreadsheets and was unable to identify who returned surveys from the first distribution. I did not have the



participant names. I identified each Registered Nurse (RN) by only a unique identifier number. We only had 8 out of 20 surveys returned after first distribution, so I did 100 percent resurvey at second survey distribution with a note attached to each survey that said if they had already completed the first survey, not to do it again. Eight additional surveys were returned from the second distribution.

The same thing occurred with Tripler Army Medical Center (TAMC); however, the Principal Investigator said after first survey distribution, that their IRB did not approve releasing names to anyone on the Research Team. It is not time for second survey distribution; however, the plan for second distribution will be the same as stated for MACH.

William Beaumont Army Medical Center's IRB process was complicated by a disagreement between two IRB members with the statistical analysis plan. The protocol was approved by the IRB, but now we are awaiting final signature by the hospital Commander. Additionally, WBAMC's IRB requested that the Army Research Institute for the Behavioral and Social Sciences (ARI) approve the WBAMC's survey, per Army Regulation 600-46, Attitude and Opinion Survey Program. The survey was approved by the ARI Chief, Army Personnel Survey Office on 14 April 2003.

Madigan Army Medical Center's local Principal Investigator requested an analysis of their MTF's responses before we do the analysis of the entire study's responses. Results pending.

Womack Army Medical Center (WAMC) had a change of Principal Investigator on 20 February 2003. Ms. Thesea Esola replaced MAJ Penny Moureau when she deployed. WAMC's IRB approval is pending, although we have received verbal approval from the IRB administrator.

There has been no published literature that definitively links the work environment or quality of care to intent to leave a job. However, my dissertation research found that one of the work environment variables, the adequacy of resources available to the bedside nurses, was associated with actually resigning from a hospital nursing job.

A twelve-month no cost extension request is being submitted to the TSNRP for review and approval. This will extend this study to 14 July 2004.

10 July 2001 to 28 May 2002: The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

We are still in the process of obtaining IRB approval at the remaining seven sites throughout the Army. Currently MAMC and TAMC have given verbal IRB approval, but we are awaiting formal notification prior to commencing the study at those sites. Because nurses at WRAMC have received too many surveys during this fiscal year, we are waiting until September to survey the NARMC, including WRAMC. Our plan at this time is to survey TAMC, MAMC and the Western Regional Medical Command (Fort Irwin and Fort Wainwright). In September, we would survey the NARMC, the South East Regional Medical Command, and the Great Plains Regional Medical Command.

There has been no published literature that definitively links the work environment or quality of care to intent to leave a job. However, my dissertation research found that one of the work environment variables, the adequacy of resources available to the bedside nurses, was associated with actually resigning from a hospital nursing job.

#### CONCLUSIONS:

There are no conclusions at this time.

## DETAIL SUMMARY SHEET

**TITLE:** Examining the Weight Management and Exercise Behaviors Among Active Duty Nursing Personnel in Maintaining Compliance with the Army's Weight Control Standards

**KEYWORDS:** weight management behaviors, exercise behaviors, self-efficacy, barriers, benefits

**PRINCIPAL INVESTIGATOR:** LTC Patricia A. Patrician, AN

**ASSOCIATES:** CPT Patricia A. Coburn AN, Barbara M. Sylvia Ph.D. RN, Col Martha Turner USAF NC

**DEPARTMENT:** Nursing  
**SERVICE:**

**STATUS:** C  
**INITIAL APPROVAL DATE:** 17 July 2001

### STUDY OBJECTIVES

This comparative descriptive study was undertaken to examine, among active duty nursing personnel, the 1) weight management and exercise behaviors, 2) perceptions of benefits and barriers to exercise, and 3) self-efficacy for exercise.

### TECHNICAL APPROACH

This study used a comparative descriptive research design to first describe the weight management and exercise behaviors, perceived benefits and barriers to exercise, and the self-efficacy to exercise in the face of barriers. Second, to compare these factors by weight category (i.e. overweight versus non-overweight). Pender's Health Promotion Model (HPM) was the organizing framework for this study. An 89-item questionnaire was distributed to nursing personnel in the National Capital Area (NCA). The questionnaire consisted of three different instruments used to examine variables that assess positive and negative weight management and exercise behaviors, determine the benefits and barriers to exercise, and determine self-efficacy expectations related to the ability to continue exercising in the face of barriers. Descriptive statistics were used to examine the data for the groups. Statistical comparisons between the groups were accomplished using Chi-square and t-tests for categorical and continuous data respectively. The Statistical Packages for Social Sciences (SPSS) v. 10.0 was used to code and analyze data.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 166.

### CONCLUSIONS

No further conclusions beyond what was reported in the previous APR.

## DETAIL SUMMARY SHEET

**TITLE:** Efficacy of Stretching and Mobilization with Neutral Wrist Splinting Versus Neutral Wrist Splinting Alone in Patients with Carpal Tunnel Syndrome: A Randomized Trial

**KEYWORDS:** Carpal Tunnel Syndrome, Nerve Conduction Studies, Randomized Trial

**PRINCIPAL INVESTIGATOR:** CPT Matt Walsworth SP

**ASSOCIATES:** MAJ Paul Pasquina, MC, CPT Jay Clasing, SP, CPT James Mills, SP

**DEPARTMENT:** Orthopaedics and Rehabilitation

**STATUS:** O

**SERVICE:** Physical Therapy

**INITIAL APPROVAL DATE:** 16 January 2001

### STUDY OBJECTIVE

To determine the efficacy of neutral wrist bracing and flexor tendon mobilization vs. wrist bracing alone in the treatment of carpal tunnel syndrome.

### TECHNICAL APPROACH

Experimental design and methods:

Subjects presenting to the physical medicine, physical therapy, or occupational therapy clinics at Walter Reed Army Medical Center and the physical therapy clinic at Kimbrough Ambulatory Care Clinic will be invited to participate in the study; after agreeing to participate, a medical history will be obtained. The history will ensure that the patient's symptoms are consistent with carpal tunnel syndrome and will rule-out the known presence of any of the exclusion criteria mentioned previously. If there is any question as to the presence of any of such exclusionary condition, the patient will be referred back to their primary care manager for appropriate examination and laboratory testing. Information will also be collected to determine the nature, duration, severity, and irritability of the patient's symptoms. Physical examination will be performed to determine presence of signs and symptoms consistent with carpal tunnel syndrome and to rule out other nerve injury in the cervical spine or upper limb. Electrophysiological examination will also be performed using standardized protocols in order to determine presence of median sensory and/or motor fiber compromise at/about the carpal tunnel region. See inclusion/exclusion criteria for more detailed descriptions of clinical and electrophysiological criteria. Those persons who meet the inclusion criteria and are willing to participate in the study will then be assigned randomly to one of the two groups ("splinting only" or "splinting and mobilization"). To randomize subjects, a computerized random number generator will be used. Odd numbers will place the subject in the exercise group and even numbers will place the subject in the splinting only group (this is considered "standard of care" for carpal tunnel syndrome). Subjects with bilateral CTS will be stratified separately and then randomized. They will then be managed in the same way with both of their wrists being assigned to the same group. Treatment will be the same regardless of limb dominance. Typically, splinting as an initial treatment for carpal tunnel syndrome could be considered the standard of care. Mobilization and splinting is more experimental, but does have some research and theoretical evidence to support use as a treatment.

Treatment for all subjects:

All patients will be given a prefabricated neutral wrist splint. Both groups will be encouraged to wear the splints as much as tolerable throughout the day and night. Subjects in each group will keep a log of the number of estimated hours per day that they wore their splint and subjects in the exercise group will keep a log of their exercise performance as well.

Treatment for the exercise group:

Exercises will be instructed by one of the researchers in the study and will be modified as needed based on the patient's response to the exercises and the physical therapist's judgment. The exercise group will be instructed in three exercises to mobilize the median nerve and flexor tendons as follows:

#### Work Unit # 01-86001 [Continued]

1. Thumb IP, MCP, CMC joint extension/abduction stretch with small range, gentle oscillations with the wrist in extension.
2. Finger DIP, PIP, and MCP joint extension stretch with small range, gentle oscillations with the wrist and elbow in extension.
3. Median neural mobilization techniques with the fingers/wrist/elbow in extension, shoulder in depression/extension, and providing gentle cervical side bending oscillations in the opposite direction.

They will perform each exercise for thirty seconds and perform two sets of each exercise during five daily exercise bouts. Subjects will be encouraged to perform the exercise with bouts spread throughout the day. Ideally, they might perform one bout in the morning upon awakening, a second bout mid-morning, the third bout at lunch, a fourth bout in the afternoon, and the final bout before going to bed in the evening. Again, a log will be used to monitor their compliance.

Follow-up and testing of all subjects:

The splinting and exercise compliance logs will be kept for six weeks. Patients will return to the clinic weekly during this time to review their compliance, address any questions or concerns, and to check and modify their exercises as indicated for the exercise group. In the event that patients are unable to attend weekly follow-ups, three of the six follow-ups may be performed by telephone. Each group will be encouraged to continue their treatment independently after the first six weeks. The CTS symptom and function questionnaires will be administered at six weeks, three months, and six months after beginning the study. Nerve conduction studies (NCS) needed for the CSI and distal median motor NCS will be performed at these same intervals. While initial electrophysiological examination is part of routine clinical practice, these follow-up nerve conduction studies are experimental and will be used to assess for change in neurophysiological function. However, EMG or NCS other than those needed to assess changes in the CSI or median motor NCS will not be performed unless there is a reason that it is clinically indicated (new or worse symptoms). Any significant increase in the symptoms will warrant discussion with the participant, appropriate medical referral, and potentially removing the subject from the study if there is electrophysiological evidence supporting further slowing of nerve conduction. Again, subjects will be allowed to remove themselves from the study at any time. Participants will be allowed to discontinue their involvement with the study at any time. Termination of the study will be at six months from entry.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

Seradge et al. conducted a prospective study to evaluate the effect of a “carpal tunnel decompression” exercise program. Twenty-eight patients (33 hands) were enrolled and participated for eighteen months. Most of the patients with mild to moderate (80% and 71% respectively) were successfully treated with this program. All patients with severe CTS required surgery. There was no control group, however, for this study.

Akalin et al. conducted a prospective randomized trial to evaluate the effect of neutral wrist splinting versus splinting and nerve and tendon gliding exercises. They enrolled 28 patients (36 hands) and followed them for 5 to 11 months. Of the patients in the splint only group 72% had good to excellent results, whereas 93% of those in the splint and exercise group had good or excellent results. However, the difference in outcomes between the groups was not statistically significant.

#### CONCLUSIONS

No enrollment.

## DETAIL SUMMARY SHEET

TITLE: The Comparison of Digital Camera Running Gait Analysis to the Telemedicine Consult System: A Pilot Study

PRINCIPAL INVESTIGATOR: Mark Jacobs, MA DOD, Shari Tomasetti M.S.

DEPARTMENT: Telemedicine  
SERVICE:

STATUS: C  
INITIAL APPROVAL DATE: 29 May 2001

### STUDY OBJECTIVE:

Research Question: In a group of study participants presenting for running gait analysis at the Pentagon Running Shoe Clinic, is there an agreement of the diagnostic finding for a participant recorded by a rater at two time points?

Expectation: We expect at least 80% agreement in diagnostic categories reviewed by a rater.

### TECHNICAL APPROACH

The first assessment, given by an Exercise Physiologist (rater), will be a Digital Video Clip (DVC) of the subject's running gait from only a lower extremity posterior view. This view protects against the identification of the subject and bias of the rater recall. Six barefoot running gait clips will be selected and stored on a Zip drive.

After the first diagnosis a running shoe will be recommended according to the diagnosis. Individuals also will be put into different weight categories. Midsole material and durability are the discriminatory features that separate shoe models for those under and over the weight guidelines. Two weeks later, the DVCs will be downloaded through the telemedicine consult system and analyzed by the same rater for a second assessment. The rater will be blinded as to which subject's DVC is being assessed, and also as to any previous diagnosis of the subject he/she is evaluating. All data will be recorded on separate data sheets and later combined into one. Second diagnosis on subjects will be compared to the initial analysis.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This experimental study observed 37% of the compared diagnosis to be equivalent. For 53% of the compared assessments, shoe recommendations were reported to be the same. There have been no amendments or modifications to the research study since the last review. These findings are noted as data collection. Nineteen subjects have been enrolled to date; there are no adverse events expected and/or serious for WRAMC site, serious AEs for other sites if multi-center study, and information on patients withdrawn from the study.

The number of subjects enrolled to the study since last APR at WRAMC is 9 and the total enrolled to date at WRAMC is 19.

There have been no publications recently printed that would affect this study.

### CONCLUSIONS

This study did not conclude the initial 80% expectancy rate of agreement in diagnostic findings. This may be due to a limited number of subject evaluations. Further studies should be done with a larger sample size and assessment of musculoskeletal injuries and pain. These variables will be more effective in evaluating this as a diagnostic procedure for preventative medicine.

## DETAIL SUMMARY SHEET

TITLE: Hepatitis G Virus and Aplastic Anemia

KEYWORDS: GBV-C/HGV, stem cell disease, aggressive viral infection, spousal co-infection

PRINCIPAL INVESTIGATOR: Jana Bednarek Ph.D. DAC

ASSOCIATES: COL KC Holtzmuller MC, DE Nicholson Ph.D.

DEPARTMENT: Clinical Investigation

STATUS: O

SERVICE: Research Operations

INITIAL APPROVAL DATE: 5 December 2000

### STUDY OBJECTIVE

The purpose of this study was to examine and determine the differences between Hepatitis G viral genomic sequences and its translation into proteins in genotypically similar HG viruses isolated from serum of an asymptomatic patient and one with serious aplastic anemia - a case study of patient and his spouse.

### TECHNICAL APPROACH

The patient's serum was obtained at the initial diagnosis and his spouse's a few days later. Both were stored at -76°C. When the protocol was approved, the patients signed informed consent form. We then prepared the hepatitis G viral RNA from the serum aliquot and stored that at -76°C as well. RNA was converted to cDNA by reverse transcription. Specific areas of the viral genome were enhanced with the use of PCR reaction and specific primers designed for this purpose. They were visualized as single bands in electrophoretic separation on agarose gel stained with ethidium bromide. For sequencing we removed PCR primers from PCR products by centrifugation using Amicon 100 filters. Purified cDNA was subjected to direct sequencing using sense or antisense primers. DNA sequencing was performed by dideoxy chain termination method using BigDye Terminator Cycle Sequencing Ready Reaction Kit (Applied Biosystems). Sequencing reaction products were purified through Centri Sep Spin columns and separated electrophoretically on Perkin Elmer ABI Prism 310 Genetic Analyzer with Power MacIntosh. Nucleotide analysis was carried out with the help of NIH program Blast.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Hepatitis G virus (HGV) has a controversial association with aplastic anemia. Our study included one patient and his spouse who developed an acute viral syndrome. The patient developed hepatitis and aplastic anemia. Both were found to be HGV RNA positive. HAV-IgM, HbsAg, anti-HBc-IgM, HCV ELISA and PCR, EBV antibodies, CMV antibodies, parvovirus IgM, HIV, ANA, ASMA were negative. Parvovirus IgG was found to have been positive eight years earlier. We sequenced 5'-Untranslated-Core-Envelope-1-Envelope-2 region, Nonstructural-3 helicase and Nonstructural-5A of both viral genomes(H and W). We have shown that the patient (H) and his spouse (W) were infected with the same HGV strain, related to PNF2161. Nucleotide composition of HGV of both the patient and his spouse were almost identical with only a few exceptions. Patient's HGV had one amino acid substitution in E2 protein that his spouse's virus and PNF2161 did not have. This was the result of one nucleotide difference. The E2 amino acid difference was located in T cell epitope, which is presented to T cells by antigen presenting cells. There were three nucleotide differences between H and W genomes in pre-core. In the recently proposed ambisense and overlapping genes that produce core-like proteins patient's HGV differed from his spouse by one amino acid in each. We were able to obtain follow-up serum from both subjects (patient and his spouse) approximately two years after the patient's bone marrow transplantation. Both were found to be positive for HGV. We sequenced all HGV genome areas as with the initial samples. Both the patient and his spouse retained the same strain of HGV and their original differences in the HGV genome nucleic acids composition.

The number of subjects enrolled to the study since last APR at WRAMC is 2 and the total enrolled to date at WRAMC is 2.

CONCLUSIONS

1. We have found small number of differences in nucleotide composition of patient (H) compared to his spouse (W) HGV genomes in the regions that we sequenced.
2. Patient had amino acid #351 serine substituted by asparagine in envelope-2 protein. This amino acid was found to be located in T cell epitope, which is presented to T cells by antigen presenting cells after processing HGV E2 protein.
3. Recently proposed ambisense and overlapping genes produce core-like proteins. Each had one amino acid change in the patient's virus compared to his spouse's (and PNF2161).
4. All glycosylation sites were preserved in E1 and E2 for both H and W, as were all cysteines.
5. All phosphorylation and myristylation sites as well as RNA binding site in helicase were preserved. Possible new phosphorylation site was introduced by threonine replacing lysine, aa #1325, the same for both H and W.
6. Polymorphism was observed in both genomes in small number of sites, particularly in helicase region, more for the spouse (W) than the patient (H).
7. Antibodies to the envelope-2 protein of HGV (Anti-HGenv), the standard assay in serum, were negative for the patient and low positive for the spouse. Presence of these antibodies is associated with recovery from HGV infection, being only transiently found simultaneously with the viral RNA.
8. In follow up, approximately two years after patient's bone marrow transplantation, we collected sera of both the patient (H) and his spouse (W). We found that they were both infected with HGV. We isolated viral RNA, prepared cDNA and sequenced the same areas of both genomes (H and W) as with the initial serum. We found that each of the subjects retained their original viral differences.

We concluded that the similarity of initial symptoms in the patient and his spouse combined with the HGV RNA findings suggest that the patient experienced an acute illness from HGV that was associated with the development of aplastic anemia.

## DETAIL SUMMARY SHEET

**TITLE:** A Prospective, Randomized, Multicenter, Open-Label, Comparative Safety and Efficacy Study of Pegasys® vs. Pegasys® Plus Ribavirin Treatment in Patients With Chronic Hepatitis C (Roche Protocol Number NR16161-E)

**PRINCIPAL INVESTIGATOR:** COL Maria H. Sjogren MC

**ASSOCIATES:** K Holtzmuller, MD; A Lindemann, RN, MS; J Friend, PA-C; P Cassarino-Lepler, LPN

**DEPARTMENT:** Clinical Investigation

**STATUS:** O

**SERVICE:**

**INITIAL APPROVAL DATE:** 23 January 2001

### STUDY OBJECTIVE

#### Primary:

To compare the safety profiles of Pegasys® plus Ribavirin vs. Pegasys® monotherapy, through week 12 (safety defined as the following adverse events: fatigue, depression, anemia, grade 3 or 4 neutropenia, or any clinically significant infections requiring treatment).

#### Secondary:

- To summarize the safety profiles of Pegasys® plus Ribavirin 24-48 weeks, and Pegasys® monotherapy for at least 12 weeks followed by Pegasys® plus Ribavirin up to week 48, through follow up (safety defined as the following adverse events: fatigue, depression, anemia, grade 3 or 4 neutropenia, or any clinically significant infections requiring treatment)
- Evaluate virologic response rate at week 12. Proportion of patients with non-detectable HCV-RNA (< 60 IU/ml by Amplicor® HCV test v2.0) or at least a 2 log-drop from screening or baseline value.
- Evaluate virologic response rates at week 24 and at 24 weeks post treatment. Proportion of patients with non-detectable HCV-RNA (< 60 IU/ml by Amplicor® HCV test v2.0).
- Summarize Serious Adverse Events (incidence, number of patients discontinued due to Serious Adverse Events, number of patients with dose adjustments due to Serious Adverse Events).
- Evaluate the predictability of week-12 HCV-RNA to week 24 and to 24 weeks post treatment response (non-detectable HCV-RNA for Pegasys® plus Ribavirin).

### TECHNICAL APPROACH

Planned program size: 1,900 subjects nationwide, 260 sites, and 10 patients at WRAMC. Patient population: Male or female patients ≥ 18 years old with serologically proven Chronic Hepatitis C. Patients should have quantifiable HCV-RNA (> 600 IU/ml by Amplicor HCV Monitor™ test version 2.0), abnormal alanine aminotransferase (ALT) and compensated liver disease, with or without cirrhosis.

This is a prospective, randomized, open-label, multicenter, safety and efficacy study. Randomization was centrally controlled. Patients were given the option of selecting one of two cohorts of patients for randomization as follows:

Cohort 1: Patients who are willing to delay treatment for 12 weeks if randomized to Arm C will be randomized into Arm A or B in a 3:1:1 ratio, respectively.

- Arm A - Pegasys® plus Ribavirin
- Arm B - Pegasys® monotherapy
- Arm C – Twelve-week treatment delay

At 12 weeks, Arm C patients will be randomized into Arm A or B in a 3:1 ratio respectively. None of the patients at WRAMC chose to select the treatment delay Arm C. Arm C was eventually dropped from the study for reasons later described.



Cohort 2: Patients who opt not to be randomized to cohort 1 because of the possibility of being randomized to a delayed treatment arm will be randomized into Arm A or B in a 3:1 ratio.

- Arm A - Pegasys® plus Ribavirin
- Arm B - Pegasys® monotherapy

The monotherapy arm, Arm B, and the treatment delay arm, Arm C, were dropped in a November 2001 addendum (approved at WRAMC January 2002). All patients were converted to combination therapy as a result of data showing Pegasys® monotherapy to be less efficient in producing a sustained virological response when compared to combination therapy with Pegasys® and Ribavirin. In January the two patients at WRAMC who had been randomized to receive Pegasys® monotherapy initiated treatment with Ribavirin.

In November 2002, the protocol was amended again due to emerging data on dosing of Ribavirin and length of treatment with respect to viral genotype. This amendment affected study design however, since none of the patients at WRAMC were affected by these changes, the new design is not described here. All patients will receive treatment for 24 to 48 weeks with an additional 24 weeks of follow up for safety. For the primary objective, Cohort 1 and Cohort 2 data will be pooled together for analysis. Subjects will be randomly assigned to treatment via an interactive voice response telephone system. Subject randomization numbers are to be allocated sequentially in each respective cohort in the order in which patients are enrolled. Randomization will be in blocks of (5) for the 3:1:1 randomization, and in blocks of (4) for the 3:1 randomization.

Discontinuation scheme:

Patients initially randomized to Arm A who did not have undetectable HCV-RNA levels (< 50 UI/ml by Amplicor® HCV test version 2.0) after 24 weeks of study treatment were considered non-responders and treatment was discontinued. However, patients with a greater than two log drop in their HCV-RNA levels from baseline to Week 24 were allowed to continue on through 48 weeks of treatment at the discretion of the investigator. Patients could continue to receive treatment through week 48 if they were initially randomized to Arm B even if HCV-RNA levels were detectable at Week 24. All patients with undetectable HCV-RNA levels at 24 weeks received an additional 24 weeks of treatment. All patients discontinuing early from study treatment completed assessment as defined for week 48 prior to follow-up.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is zero and the total enrolled to date at WRAMC is ten. None of the subjects enrolled at WRAMC withdrew from the study. The total number enrolled study-wide is 1,887 at 227 sites. Enrollment is now closed study-wide. The FDA approved Pegasys® for commercial use in September 2002.

Following is a protocol amendment/addenda history in reverse chronological order:

Amendment E approved 10/17/02 - Based on data from another Roche phase III combination therapy trial, this amendment was submitted for review. The results from this study showed that:

- Patients with genotype 1 had higher sustained virological responses when treated with 1000 or 1200 mg of Ribavirin for 48 weeks than when treated either for less time (24 weeks) or with a lower dose of Ribavirin (800mg).
- Patients with genotype non-1 achieved a similar sustained virological response regardless of treatment duration or Ribavirin dose. Thus the benefits can be obtained while lowering the risks associated with a longer duration of treatment.

Due to these data, this protocol was amended to increase the Ribavirin dose for genotype 1 patients from 800mg to either 1000mg or 1200mg based on weight, and decrease the treatment duration for genotype non-1 patients to 24 weeks regardless of virological response. Additionally, the protocol is being amended to allow genotype 1 patients to continue treatment through 48 weeks if there is a log 2 drop in HCV RNA from baseline to week 24 where previously they would have been discontinued from treatment at week 24. This amendment had no effect on any patients at WRAMC as all patients had completed the therapy portion of the protocol by the time of IRB approval.

Addendum approved 07/02/02 - Enrollment closed study wide.

Addendum approved 03/01/02 - Investigators Brochure Version #6-December 2001 and patient diary submitted.

Amendment D approved 01/04/02 - The monotherapy arm, Arm B, and the treatment delay arm, Arm C, were dropped and all patients were converted to combination therapy as a result of data that showed Pegasys® monotherapy to be less efficient in producing a sustained virological response when compared to combination therapy with Pegasys® and Ribavirin. In January 2002 the two patients at WRAMC who had been randomized to receive Pegasys® monotherapy initiated treatment with Ribavirin.

The following serious adverse events have been reported during this study since the last APR and none of these events occurred at WRAMC. All are from different clinical trials with the exception of the event dated 11/08/01(MCN264609) that was from this trial but at a different clinical site. All events were reported to IRB as they were received by this facility. The summary of these adverse events is provided in reverse chronological order:

Adverse Event 10/21/02 (MCN 314915)-Downgrading of previously reported AE for Aseptic Meningitis whose causality was changed to unrelated for both Peginterferon alfa-2a and for Ribavirin due to additional follow up data

Adverse Event 10/08/02 (MCN321278)-Death due to thrombotic thrombocytopenic purpura

Adverse Event 08/23/02 (MCN311789)-Transient left 6<sup>th</sup> cranial nerve palsy with diplopia

Adverse Event 06/27/02 (MCN263869)-Osteomyelitis following ingrown toenail left foot

Adverse Event 06/25/02 (MCN314915)-Aseptic Meningitis

Adverse Event 05/15/02 (MCN312571)-Celiac Sprue

Adverse Event 03/15/02 (MCN308224)-Ganglionic tuberculosis

Adverse Event 12/05/01 (MCN302091)-Thyroid Cysts

Adverse Event 11/08/01 (MCN264609)-Rhabdomyolysis

No serious adverse events occurred in any WRAMC patients taking part in this protocol. However, all experienced at least one adverse event. These adverse events were coded as mild to moderate and in general responded to dosage adjustments and/or treatment for the adverse event. Most commonly fatigue was reported affecting 9/10 participants. Six out of ten were affected by mood changes or depression. Three patients required dosage modifications due to neutropenia. Three patients had mild anemia, none of which required dosage adjustments for the anemia. Two patients had significant weight loss. One patient has a new onset post-nasal drip. Seven out of ten reported minor infections some of which required treatment with antiviral or antibiotic medications. These infections included bronchitis, URI, flu, eye, ear, pneumonia, folliculitis, cellulitis, and UTI. Other reported adverse events included insomnia, generalized itching, headaches, and myalgias/arthralgias.

### CONCLUSIONS

Out of ten enrolled subjects, all have completed the therapy portion of the protocol. Two discontinued at Treatment Week 24 per protocol due to detectable hepatitis C virus. These two patients have also completed the 24-week follow up phase of the protocol. Of the remaining eight subjects, all of whom completed 48 weeks of therapy, one had detectable virus at Week 48 and one had detectable virus at three months follow up. The other six subjects are at various points of follow up and continue to show a virological response to therapy. The last follow up visit is scheduled in April 2003. This 60% response rate is consistent with rates of sustained virological response as reported in the literature, however, data is still unavailable for Follow up Week 24 for all patients who completed 48 full weeks of therapy and therefore any further analysis of these results is premature.

## DETAIL SUMMARY SHEET

TITLE: A Prospective, Randomized, Multicenter, Open-Label, Comparative Safety and Efficacy Study of Pegasys® vs. Pegasys® Plus Ribavirin Treatment in Patients With Chronic Hepatitis C. (Roche Protocol Number NR16161-E)

PRINCIPAL INVESTIGATOR: COL Maria H. Sjogren MC

ASSOCIATES: Kent Holtzmuller, MD, Julia Friend, PA-C, Pia Cassarino-Lepler, LPN

DEPARTMENT: Clinical Investigation

STATUS: C

SERVICE:

INITIAL APPROVAL DATE: 23 January 2001

### STUDY OBJECTIVE

Primary:

- To compare the safety profiles of Pegasys® plus Ribavirin vs. Pegasys® monotherapy, through week 12 (safety defined as the following adverse events: fatigue, depression, anemia, grade 3 or 4 neutropenia, or any clinically significant infections requiring treatment).

Secondary:

- To summarize the safety profiles of Pegasys® plus Ribavirin 24-48 weeks, and Pegasys® monotherapy for at least 12 weeks followed by Pegasys® plus Ribavirin up to week 48, through follow up (safety defined as the following adverse events: fatigue, depression, anemia, grade 3 or 4 neutropenia, or any clinically significant infections requiring treatment)
- Evaluate virologic response rate at week 12. Proportion of patients with non-detectable HCV-RNA (< 60 IU/ml by Amplicor® HCV test v2.0) or at least a 2 log-drop from screening or baseline value.
- Evaluate virologic response rates at week 24 and at 24 weeks post treatment. Proportion of patients with non-detectable HCV-RNA (< 60 IU/ml by Amplicor® HCV test v2.0).
- Summarize Serious Adverse Events (incidence, number of patients discontinued due to Serious Adverse Events, number of patients with dose adjustments due to Serious Adverse Events).
- Evaluate the predictability of week-12 HCV-RNA to week 24 and to 24 weeks post treatment response (non-detectable HCV-RNA for Pegasys® plus Ribavirin).

### TECHNICAL APPROACH

Planned program size: 1,900 subjects nationwide, 260 sites, 10 patients at WRAMC.

Patient population: Male or female patients ≥ 18 years old with serologically proven Chronic Hepatitis C.

Patients should have quantifiable HCV-RNA (> 600 IU/ml by Amplicor HCV Monitor™ test v2.0), abnormal alanine aminotransferase (ALT) and compensated liver disease, with or without cirrhosis.

This is a prospective, randomized, open-label, multicenter, safety and efficacy study. Randomization was centrally controlled. Patients were given the option of selecting one of two cohorts of patients for randomization, as follows:

Cohort 1: Patients who are willing to delay treatment for 12 weeks if randomized to Arm C, will be randomized into Arm A or B in a 3:1:1 ratio, respectively.

- Arm A - Pegasys® plus Ribavirin
- Arm B - Pegasys® monotherapy
- Arm C - Twelve-week treatment delay

At 12 weeks, Arm C patients will be randomized into Arm A or B in a 3:1 ratio, respectively.

None of the patients at WRAMC chose to select the treatment delay Arm C. Arm C was eventually dropped from the study for reasons later described.

Cohort 2: Patients who opt not to be randomized to cohort 1 because of the possibility of being randomized to a delayed treatment arm will be randomized into Arm A or B in a 3:1 ratio.

- Arm A - Pegasys® plus Ribavirin
- Arm B - Pegasys® monotherapy

The monotherapy arm, Arm B, and the treatment delay arm, Arm C, were dropped in a November 2001 addendum (approved at WRAMC January 2002). All patients were converted to combination therapy as a result of data that showed Pegasys® monotherapy to be less efficient in producing a sustained virological response when compared to combination therapy with Pegasys® and Ribavirin. In January the two patients at WRAMC who had been randomized to receive Pegasys® monotherapy initiated treatment with Ribavirin.

In November 2002, the protocol was amended again due to emerging data on dosing of Ribavirin and length of treatment with respect to viral genotype. This amendment affected study design however, since none of the patients at WRAMC were affected by these changes, the new design is not described here. A summary of the November 2002 amendment was provided in the 12/06/02 annual progress report. All patients received treatment for 24 to 48 weeks with an additional 24 weeks of follow up for safety.

For the primary objective, Cohort 1 and Cohort 2 data will be pooled together for analysis. Subjects will be randomly assigned to treatment via an interactive voice response telephone system. Subject randomization numbers are to be allocated sequentially in each respective cohort in the order in which patients are enrolled. Randomization will be in blocks of (5) for the 3:1:1 randomization, and in blocks of (4) for the 3:1 randomization.

Discontinuation scheme:

Patients initially randomized to Arm A who did not have undetectable HCV-RNA levels (< 50 UI/ml by Amplicor® HCV test v2.0) after 24 weeks of study treatment were considered non-responders and treatment was discontinued. However, patients with a greater than two log drop in their HCV-RNA levels from baseline to Week 24 were allowed to continue on through 48 weeks of treatment at the discretion of the investigator. Patients could continue to receive treatment through week 48 if they were initially randomized to Arm B even if HCV-RNA levels were detectable at Week 24. All patients with undetectable HCV-RNA levels at 24 weeks received an additional 24 weeks of treatment. All patients discontinuing early from study treatment completed assessment as defined for week 48 prior to follow-up.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is zero and the total enrolled to date at WRAMC is ten. None of the subjects enrolled at WRAMC withdrew from the study. All subjects have completed all scheduled treatment and follow up visits. The total number enrolled study-wide was 1,887 at 227 sites. Enrollment is closed study-wide.

Following is a protocol amendment/addenda history since the last APR in reverse chronological order:

Addendum 12/12/02 - The U.S. FDA has approved combination therapy with Pegasys® (pegylated interferon alfa-2a) and Copegus® (Ribavirin) for the treatment of adults with chronic hepatitis C who have compensated liver disease and who have not previously been treated with interferon alpha. The Investigator Drug Brochure was updated to reflect this.

The following serious adverse events have been reported during this study since the last APR; none of these events occurred at WRAMC. All are from different clinical trials. All events were reported to IRB as they were received by this facility. The summary of these adverse events is provided in reverse chronological order:

Adverse Event report dated 6/6/03 (IND Safety Report MCN #331169)- unexplained death

Adverse Event report dated 5/23/03 (IND Safety Report MCN #331169)- unexplained death

#### Work Unit # 01-92002 [*Continued*]

Adverse Event report dated 3/24/03 and Follow up report dated 5/7/03 (IND Safety Report MCN #333092)-unexplained death

Adverse Event report dated 02/21/03 (IND Safety Report MCN #331169)- Non Hodgkin's Lymphoma

Adverse Event report 12/09/02 (IND Safety Report MCN #325741)-Cerebral Atrophy

Adverse Event report dated 12/09/02 (IND Safety Report MCN #261158)-Follow up of previously reported avascular necrosis of hip bone. Follow up x-rays revealed normal hip bone x-rays; patient had residual pain.

No serious adverse events occurred in any WRAMC patients taking part in this protocol; however, all experienced at least one expected adverse event. These adverse events were coded as mild to moderate and in general responded to dosage adjustments and/or treatment for the adverse event. Most commonly fatigue was reported affecting 9/10 participants. 6/10 were affected by mood changes or depression. Three patients required dosage modifications due to neutropenia. Three patients had mild anemia, none of which required dosage adjustments for the anemia. Two patients had significant weight loss. One patient has a new onset post-nasal drip. Seven out of ten reported minor infections some of which required treatment with antiviral or antibiotic medications. These infections included bronchitis, URI, flu, eye, ear, pneumonia, folliculitis, cellulitis, and UTI. Other reported adverse events included insomnia, generalized itching, headaches, and myalgias/arthralgias.

#### CONCLUSIONS

Out of ten enrolled subjects at WRAMC, all have completed the therapy portion and follow up portions of the protocol. Two patients discontinued at Treatment Week 24 per protocol due to detectable hepatitis C virus. The remaining eight subjects each completed 48 weeks of therapy and an additional 24 weeks of follow up. Of these eight subjects, four achieved sustained virological response to treatment and had undetectable levels of hepatitis C six months after treatment completion. One patient never showed a virological response having detectable virus at Week 48. Three subjects relapsed having detectable virus at three or six months follow up. This 40% response rate is consistent with rates of sustained virological response as reported in the literature; however, data analysis study-wide is ongoing.

## DETAIL SUMMARY SHEET

TITLE: Hepatitis C Virus Infection: Mechanism of Disease Progression

KEYWORDS: Hepatitis C; virus; liver; cirrhosis; HCV RNA; epidemiology; US military

PRINCIPAL INVESTIGATOR: Sjogren, Maria COL MC

DEPARTMENT: Clinical Investigation

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 20 February 2001

### STUDY OBJECTIVE

The principal hypothesis of this study is that active duty members infected with HCV genotype 1 liver disease progress more rapidly than in subjects infected with non-HCV non-genotype 1. Assessment on other variables which might influence histologic progression of liver disease including age, race, rank, deployment, and alcohol consumption. HCV RNA level will be determined as well.

Specific objectives are as follow:

1. To compare the rate of progression of liver disease based on histologic severity scale in military subjects infected with genotype 1 to the rate of progression in those infected with non-genotype 1.
2. To identify other predictors of histologic liver disease.
3. To determine risk factors for acquisition of genotype-1 compared to non-genotype 1 HCV.
4. To describe the natural history of HCV infection in a large group of a military population, including morbidity and mortality.

### TECHNICAL APPROACH

This is a study of active duty military men or women who have the diagnosis of chronic HCV infection. Eligible subjects who seek medical care at the Gastroenterology Service/Liver Clinic for HCV infection are informed about this study by the principal investigator or clinical trial coordinator. Clinical status (status of liver disease, presence of co-morbid medical conditions, markers of hepatic synthetic function) and a serum sample stored at - 70 °C for future analysis will be assessed at follow-up visits every six months. Questionnaires will be administered every six months regarding ongoing risk factors for HCV infection and quality of life (modified SF-36, CLDQ-HCV).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 15 and the total enrolled to date at WRAMC is 56. There are 48 active participants, 2 are deceased, and 6 terminated participation early. Those who terminated cited reasons including "too far to travel" and one felt the "questions were not relevant". The others were lost to follow up. Enrollment is open and ongoing. We hope to accrue 300 patients total. This goal may require downward adjusting in part due to the loss of Balboa Medical Center as an expected participating site. This is not an interventional study. No adverse events have been reported since the last APR.

At this point, no subjects have completed the study, and none are expected to complete it for another 2.5 years. Therefore, inferences cannot be made about histological progression until there is complete study data including the second liver biopsy. However, the existing sample can be described as follows:

#### Sample Demographics:

- 83% of the sample is male.
- 42% of the sample is under 40. The mean age is 40.
- 25% are African American. 65% are Caucasian, 8% are Latino, and 2% are Asian.
- 21% completed high school, 60% had at least some college, and 19% of the sample had post-graduate work.

Work Unit # 01-92003 [*Continued*]

- 52% had a household income of >\$50,000, 37% had a household income of \$25,000-50,000, and 10% had a household income between \$10,000-25,000.
- 75% of the sample is enlisted.
- 39% think they have had HCV for at least 10 years; 23% think they have had it less than 10 years.

Baseline Lab/Histology Data:

By and large, the sample does not have indicators of advanced (decompensated) liver disease as evidenced by biochemical indicators. The mean PT is 13.6, mean albumin is 4.05, and mean ALT is 90.

- 50% of the sample had ALT less than 72, which is the high limit for males at WRAMC laboratories.
- 76% of the sample is genotype-1 and 24% is genotype non-1.
- 62% of the sample had viral loads >500,000 IU/mL, 18% of the sample had viral loads >850,000 IU/mL.
- 56% of the sample had little or no fibrosis, 27% had bridging fibrosis, and 10% were cirrhotic or progressing to cirrhosis on biopsy.

Lifestyle Factors potentially contributing to disease acquisition or progression:

- 14% of the sample self reports having a drinking problem now or in the past.
- 20% of the sample currently drinks alcohol at least once per week, 54% are abstainers.
- 10% have had a DUI.
- 30% answered one of the CAGE questions affirmatively.
- 60% of this sample has a tobacco use history, but only 27% are current smokers.
- 17% have been incarcerated.
- 39% have had more than 10 sexual partners.
- 17% have had sexual intercourse with a prostitute.

Risk Factor Analysis:

- 20% of the sample has a prior history of blood transfusion.
- 48% have had at least one body piercing.
- 46% are tattooed.
- 14% have had acupuncture.
- 4% have had needle sticks.
- 10% have a past history of IV Drug Use.
- 60% report having had cutaneous exposure to somebody else's blood.
- 64% shared nail trimming instruments.

We were able to examine this preliminary data to see if any trends or patterns emerged, specifically with respect to our aim of determining if there were any specific risk factors for acquisition of genotype 1 compared to non-genotype 1 HCV. An analysis looking at the relationship between genotype, demographics and risk factors revealed that 64% of officers had a non-1 genotype while 88% of enlisted subjects were genotype 1. This difference was significant at  $p<.001$ . Additionally, 73% of subjects with tattoos were infected with a non-1 genotype, while only 27% of subjects without tattoos had a non-1 genotype. This difference was significant at  $p=.048$ . This was an unexpected and interesting finding.

Quality of Life:

- 19% of the sample feels that they have been limited by their HCV in the past two weeks in performing their daily work at least some of the time during the past two weeks.
- 19% of the sample feels that their HCV has limited their activities (walking, climbing stairs, carrying groceries, playing sports) at least some of the time in the last two weeks.
- 38% of the sample worried at least some of the time during the past two weeks that their symptoms will develop into major problems.

Work Unit # 01-92003 [*Continued*]

- 36% of the sample worried at least some of the time during the past two weeks that they might die earlier than expected because of their Hepatitis C.
- 55% of the sample worried at least some of the time over the previous two weeks about the impact hepatitis C has on their family.
- 30% of the sample experienced emotional stress or strain in their relationships at least some of the time during the past two weeks as a result of their hepatitis C.

These data are generated from the chronic liver disease questionnaire-HCV (CLDQ-HCV) which is asked at baseline and each patient visit. The SF-36 or Hepatitis Quality of Life Questionnaire (HQLQ) is also administered at each visit. Upon completion of the study, HQLQ data will be scored by a professional scoring service, therefore, no analysis is available at the time of this report.

### CONCLUSIONS

Inferences cannot be made about histological progression of hepatitis C in this population until there is more complete study data including the second liver biopsy. However, some interesting and significant correlations were revealed with respect to genotype and military rank and genotype and presence of tattoos. As more data points are obtained, analysis that looks at other indicators of disease progression such as biochemical markers will also be able to be performed. Additionally, it is hoped that the morbidity and quality of life data will lend insight into an under-researched area of study in this disease process.



## DETAIL SUMMARY SHEET

TITLE: Interleukin-6 and Tumor Necrosis Factor-alpha Role In Alcoholic Liver Cirrhosis

KEYWORDS:

PRINCIPAL INVESTIGATOR: Marcos Rojkind, MD, Ph.D.

ASSOCIATES:

DEPARTMENT: Clinical Investigation  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 14 September 2001

### STUDY OBJECTIVE:

To determine the role of the acute phase response and the cytokines of the acute phase response on collagen gene expression in the liver. Although this protocol overlaps with protocol 01-92005, it was submitted as a means to start the experimental part in vitro using cell cultures. No animal usage is contemplated for this particular protocol. Prior to receiving approval for animal usage (see protocol 01-92005) this protocol allowed the PI to start his work and comply with the requirements of NIH, the sponsoring institution for this grant proposal.

### TECHNICAL APPROACH:

Analyze the molecular mechanisms whereby the cytokines of the acute phase response modulate the expression of collagen and matrix metalloproteinase mRNA by hepatic stellate cells.

### PRIOR AND CURRENT PROGRESS:

We have made significant progress in this area. Combining experiments performed under the aegis of this and 01-92005 Working Units, we have completed various papers. Two have been already published in the American Journal of Pathology and FEB letters and copies of the manuscripts were added to the APR. An additional manuscript has been submitted to the American Journal of Physiology. This article is being revised for re-submission.

### CONCLUSIONS:

Our findings demonstrated that the type I collagen genes and matrix metalloproteinase-13 mRNAs are reciprocally modulated. We also showed that MMP-13 is only expressed by HSC and not by hepatocytes. We also found that TGF- $\beta$ 1 up-regulates the expression of MMP-13 mRNA approximately 12-24 hours after exerting its fibrogenic effect on type I collagen genes. We further showed that while p38 MAPK is required for MMP-13 mRNA up-regulation, ERK1/2K down-regulates its expression. We also found that while TGF- $\beta$ 1 induces a delayed proliferative response in HSC, TNF- $\alpha$  abrogates this TGF- $\beta$ 1-mediated action. A manuscript containing this information is being prepared for publication.

## DETAIL SUMMARY SHEET

TITLE: The Role of the Acute Phase Response in Alcoholic Liver Cirrhosis

KEYWORDS:

PRINCIPAL INVESTIGATOR: Marcos Rojkind, MD, Ph.D.

ASSOCIATES:

DEPARTMENT: Clinical Investigation

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 14 September 2001

### STUDY OBJECTIVE:

To determine the role of the acute phase and the cytokines of the acute phase response on collagen gene expression in the liver of rats fed alcohol. This protocol overlaps in experimental details with protocol 01-92004. However, in this protocol we need to perform the experiments with cells isolated from the animals fed alcohol. Although the veterinarian of AFIP has approved the animal studies, at this time it is impossible to keep animals in their facility. Therefore, the performance of animal studies is postponed until we obtain permission from USUHS to keep our animals in their facility. Nonetheless, we have made significant progress in our "in vitro" studies using the various cell lines that we developed and will be reported in protocol 01-92004.

### TECHNICAL APPROACH:

For these experiments we need to administer ethanol by gavage to rats receiving endotoxin and/or kept in a choline-deficient diet. In previous studies, we have already reported the changes in blood acute phase cytokines and leptin. In this protocol, we propose to investigate the effect of alcohol and endotoxin on the expression of extracellular matrix genes by isolated hepatic stellate cells. These experiments will be performed as soon as we have the permission of USUHS to perform these studies and to use their facility to keep the rats.

### PRIOR AND CURRENT PROGRESS:

Because of our difficulties with AFIP, we are carrying out the paperwork necessary to get approval from USUHS to perform animal studies and to maintain the animals in their facility. As soon as we obtain their permission and CIC approval, we shall start the animal experiments. The grant that covers the expenses of these studies is approved until April of 2005.

### CONCLUSIONS:

Based on our previous progress report and our publications prior to joining WRAMC, our data strongly suggest that ethanol feeding to rats induces an oxidative stress response that, if supplemented by acute phase episodes such as it occurs in patients with alcoholic hepatitis, the development of liver fibrosis is accelerated and there is more collagen deposited in the livers of rats. This suggests that any superimposed pathology that causes an acute phase response in patients with chronic liver disease could accelerate the development of liver fibrosis.

## DETAIL SUMMARY SHEET

TITLE: Alcohol-induced Liver Fibrosis: An In Vitro Model

KEYWORDS:

PRINCIPAL INVESTIGATOR: Marcos Rojkind, MD, Ph.D.

ASSOCIATES:

DEPARTMENT: Clinical Investigation  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 14 September 2001

### STUDY OBJECTIVE:

To study the effects of ethanol and its metabolite acetaldehyde on collagen and collagenase gene regulation.

### TECHNICAL APPROACH:

For these studies the PI took advantage of the numerous hepatic stellate cell lines developed in our laboratory and a human cell line provided by investigators of the Mount Sinai School of Medicine in New York. These cultured cells are treated with acetaldehyde or the fibrogenic cytokine TGF- $\beta$ 1 and harvested at various time-points for total RNA extraction and determination of mRNA expression by semiquantitative PCR. In some instances, total protein is also extracted and the expression of transcription factors or the activity of specific protein kinases determined by Western blotting.

### PRIOR AND CURRENT PROGRESS:

We have made significant progress in this area. Combining experiments performed under the aegis of this and 01-92005 Working Units, we have completed various papers. Two have been already published in the American Journal of Pathology and FEB letters and copies of the manuscripts were provided with the APR. An additional manuscript has been submitted to the American Journal of Physiology. This article is being revised for re-submission.

### CONCLUSIONS:

Our findings demonstrated that the type I collagen genes and matrix metalloproteinase-13 mRNAs are reciprocally modulated. We also showed that MMP-13 is only expressed by HSC and not by hepatocytes. We also found that TGF- $\beta$ 1 up-regulates the expression of MMP-13 mRNA approximately 12-24 hours after exerting its fibrogenic effect on type I collagen genes. We further showed that while p38 MAPK is required for MMP-13 mRNA up-regulation, ERK1/2K down-regulates its expression.

## DETAIL SUMMARY SHEET

TITLE: S000A – Prevention of Alzheimer’s Disease with Vitamin E and Selenium (PREADVISE) Phase III  
Ancillary to S0000 - SELECT

KEYWORDS: Memory, Alzheimer’s disease, Prevention, Neurodegenerative disease, Dementia  
PRINCIPAL INVESTIGATOR: Robert C. Dean LTC MC (deployed) (Moul, Judd W., COL MC)

ASSOCIATES: Judd W. Moul COL MC, Margaret M. Swanberg MAJ MC, Kevin Cannard LTC MC, Mark P. Kelly, Ph.D., Kimberly A. Peay, NP

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: O  
INITIAL APPROVAL DATE: 30 July 2002

### STUDY OBJECTIVE:

The primary objective is to define the effect of selenium and vitamin E in combination in the reduction of the incidence of Alzheimer’s disease (AD), as determined by mental status screening and clinical evaluation, in a population of men age 62 or older (60 if African descent or Hispanic) participating in SELECT. Secondary objectives are: to define the effect of selenium and vitamin E alone in the reduction of the incidence of Alzheimer’s disease, in a population of men age 62 or older (60 if of African descent or Hispanic) participating in SELECT; to assess the combined and individual effects of selenium and vitamin E in the reduction of the incidence of other neurodegenerative diseases, including dementia with Lewy bodies, frontotemporal dementia (including Pick’s disease), corticobasal degeneration, progressive supranuclear palsy, and vascular dementia; to evaluate the sensitivity and specificity of the Memory Impairment Screen (MIS) relative to the Consortium to Establish a Registry in AD (CERAD) mental status measures (in a sub-sample of 500 participants); to study the features of normal cognitive aging (in a sub-sample) and to assess the effect of selenium and vitamin E on this process; and to study the progression of AD and other neurodegenerative diseases in participants clinically diagnosed with AD or other dementia. The tertiary objective is to evaluate the association of apolipoprotein E (APOE) and 4 alleles and other potential biological molecular markers with the risk of Alzheimer’s disease and other neurodegenerative diseases in this population.

### TECHNICAL APPROACH

Participants who are enrolled in SELECT SWOG S1000A (WU #01-28001) and who are 62 years or older (age 60 for men of African descent or Hispanic) who score higher than 4 on the Memory Impairment Screen (MIS) and who have no history of Alzheimer’s disease or other forms of dementia, who have had no head injury with prolonged loss of consciousness (over 30 minutes) within the past five years, who have had no alcohol or substance abuse in the past 24 months, who are not taking aricept, cognex, exelon, reminyl or hydergine, and who are not blind, deaf, or have language difficulties or any other disability that may prevent completion of the MIS are eligible. If AD or another dementia is diagnosed, the participant will be reevaluated with the CERAD measures on an annual basis until the participant is no longer able to comply with the PREADVISE study procedures. If dementia is not diagnosed, the participant will be followed with the proposed screening methods starting with the MIS at the next SELECT annual visit.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been none. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

There have been no conclusions to date.

## DETAIL SUMMARY SHEET

TITLE: A Prospective Randomized Trial of Post-Exposure Prophylaxis for Anthrax

KEYWORDS: anthrax

PRINCIPAL INVESTIGATOR: Duncan, William COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: General Medicine

INITIAL APPROVAL DATE: 30 October 2001

### STUDY OBJECTIVE

To prospectively collect data about patients exposed to anthrax spores and then perform studies to identify medistinal inflammation in patients at risk for inhalational anthrax.

### TECHNICAL APPROACH

The protocol is unchanged (no modifications).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No patients have been enrolled in this protocol – this protocol is being put in place in the event of another anthrax mailing.

The number of subjects enrolled to the study since last APR is 0, and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

None.

## DETAIL SUMMARY SHEET

**TITLE:** Does the Combination of Pirfenidone, Enalapril, and Lovastatin Reduce Proteinuria and Glomerular/Interstitial Histologic Score in Rats with PAN-Induced FSGS and Existing Nephrotic Syndrome?

**KEYWORDS:** FSGS, pirfenidone, angiotensin converting enzyme inhibitors

**PRINCIPAL INVESTIGATOR:** Yuan, Christine, LTC, MC

**ASSOCIATES:** Mrs. Luana Kiandoli, Dr. Sharda Sabnis, Christopher Glanton, CPT, MC

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Nephrology

**INITIAL APPROVAL DATE:** 13 November 2001

**STUDY OBJECTIVE:** The hypothesis of the study is to show that combination therapy with Pirfenidone, Enalapril and Lovastatin, begun after the onset of overt proteinuria (i.e. 12 weeks) in rats with PAN-induced FSGS will result in the following as compared to positive controls:

- Preserved glomerular and tubulointerstitial histology (primary outcome)
- Reduction in proteinuria (primary outcome)
- Preserved creatinine clearance (primary outcome)
- Decreased expression of mRNA for TGF- $\beta$  (secondary outcome; to be pursued only if histologic improvement is present)
- Preserved serum creatinine, higher albumin, and lower cholesterol

**TECHNICAL APPROACH:** This study will be a randomized, prospective controlled trial. Forty-four male Sprague-Dawley rats will be used. There will be one normal control group, and three groups of rats with PAN-induced FSGS. Two of these “diseased” groups will receive treatment with either Enalapril/Lovastatin/Pirfenidone or Enalapril/Lovastatin, beginning at 12 weeks after PAN-induction. Twelve weeks after FSGS is induced, 24-hour urine protein will be measured in all groups. At this point, treatment will be initiated in two of the three rat groups with disease, with the extra group being a positive, “diseased” control. The fourth group of rats that do not have disease induction will serve as normal controls. At 18 weeks, twenty-four hour urine protein and creatinine, serum creatinine, cholesterol, and albumin will be measured, after which all rats will be euthanized. Renal tissue from the rats will be examined for histopathologic evidence of focal segmental glomerulosclerosis, and this along with proteinuria, will be the primary outcome variable. RNA will be extracted from the renal cortical tissue, frozen, and retained for further analysis of TGF  $\beta$  mRNA pending outcome of renal histology.

**PRIOR AND CURRENT PROGRESS:** Forty-four rats were entered into the study at AFIP. All survived up until week 12, at which time therapy was begun with lovastatin, enalapril, and +/- pirfenidone. After week 12, 2 animals in the enalapril/lovastatin group, 1 animal in the positive control group, and 1 animal in the enalapril/lovastatin/pirfenidone group were euthanized or expired between weeks 13 and 15 due to weight loss, volume depletion, and poor condition. This was after assessment by the AFIP veterinarian. 2/4 in whom renal function was determined had a very elevated serum creatinine. All other animals survived until the time of scheduled euthanasia at week 18 in July 2002. At present, analysis of blood and urine chemistries, and preparation of renal tissue for pathologic review is ongoing.

**CONCLUSIONS:**

Pending analysis of blood, urine, and renal tissue.

## DETAIL SUMMARY SHEET

**TITLE:** The Effects of Ovarian Steroids on the Responsiveness of Mouse Renal Medullary Cells to Vasopressin

**KEYWORDS:** ovarian steroids, Vasopressin, receptors

**PRINCIPAL INVESTIGATOR:** Yuan, Christine, LTC, MC

**ASSOCIATES:** Mrs. Luana Kiandoli; CPT M. Gray Napier

**DEPARTMENT:** Medicine

**SERVICE:** Nephrology

**STATUS:** O

**INITIAL APPROVAL DATE:** 13 November 2001

**STUDY OBJECTIVE:** Previous studies have shown that ovarian hormones decrease the responsiveness of rat medullary collecting cells to Vasopressin stimulation in vitro. Although estrogen incubation decreases cAMP levels in rat renal medullary cells, and female rats have lower Vasopressin (V2) receptor density than male rats; the direct effects of ovarian steroids on V2 receptor expression and density have not been evaluated. The purpose of this study is to determine how estrogen produces an inhibitory effect on Vasopressin responsiveness. We hypothesize that estrogen decreases Vasopressin (V2) receptor density leading to decreased signal transduction.

**TECHNICAL APPROACH:** Mouse renal medullary cells have been shown to retain many characteristics of cortical collecting duct cells including responsiveness to arginine Vasopressin. Using these cells, we will determine the effects of low, medium, and high concentrations of estrogen and progesterone, as well as a combination of intermediate concentrations of estrogen and progesterone on Vasopressin (V2) receptor membrane density. Cells exposed to estrogen and progesterone will also be stimulated with Vasopressin, and cAMP levels will be measured, to provide a functional correlate with V2 receptor density. Each experimental condition will be run in triplicate. Therefore, the primary variable to be measured will be: 1) AVP V2 receptor membrane density as a function of ovarian steroid hormone type (i.e., estrogen or progesterone) and ovarian steroid concentration; 2) cAMP production as a functional measure of V2 receptor response to AVP, post ovarian steroid hormone stimulation.

**PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE:** Vasopressin stimulation experiments have been performed, with cAMP production present in controls (indicating functional receptors are present), and suppressed with the addition of estrogen and progesterone in a dose dependent manner. We are presently doing the experiments to determine receptor membrane density. Initial experiments, using a method validated in the literature, were unsuccessful—and we have made some modifications, specifically using the same ligand to determine non-specific binding, and total binding (i.e., tritium-labeled vs. “cold”). The original paper employed Vasopressin as the “cold” ligand, and another, much more tightly binding ligand as the radiotracer ligand, probably limiting non-specific binding. We anticipate completion in the December/January time frame. This is a cell-culture study. There are no human or animal subjects. There are no recent experiments reported in the literature that would change our protocol.

The number of subjects enrolled to the study since last APR at WRAMC is NA and the total enrolled to date at WRAMC is NA.

**CONCLUSIONS:**

Please see progress section above.

## DETAIL SUMMARY SHEET

TITLE: Is Delayed Gastric Motility Associated with Impaired Absorption of Tacrolimus in Diabetic Organ Transplant Recipients?

KEYWORDS:

PRINCIPAL INVESTIGATOR: Yuan, Christina LTC MC

ASSOCIATES:

DEPARTMENT: Medicine

SERVICE: Nephrology

STATUS: O

INITIAL APPROVAL DATE: 29 January 2002

### STUDY OBJECTIVE:

The objective of this study is to test whether there is reduced Tacrolimus (FK-506) bioavailability in diabetics after transplant and if so, if it is associated with delayed gastric motility, theoretically by allowing increased contact time and thus increased metabolism by the intestinal Cytochrome P450 3A4 system that predominates in the upper GI tract.

### TECHNICAL APPROACH:

We will evaluate a sample of diabetic transplant recipients for alterations in the tacrolimus area-under-the-curve (AUC, a measure of tacrolimus pharmacokinetics) and determine the incidence of gastric dysmotility among that sample compared to non-diabetic controls. There will be 10 subjects in each group. Once the AUC data is obtained, it will be analyzed to determine if a statistically significant difference is present between diabetics and non-diabetics. If a statistically significant difference exists between groups, all patients will be asked to contact the Nuclear imaging department at WRAMC and schedule a time to perform the Nuclear Scintigraphy to determine the incidence of delayed gastric emptying among the two groups.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 12 and the total enrolled to date at WRAMC is 12. Eight non-diabetic subjects have been entered; and 4 diabetic subjects. We have performed AUC's on these 12 subjects, and there has been 1 "flat" AUC in each group. Completion of both arms should occur within the next year. No subjects have yet had the gastric emptying study, because the AUC arm is not yet complete. There have been no adverse events. There are no final conclusions yet available. There is no new recent literature that would render the study not worth doing.

### CONCLUSIONS:

None available as yet.



## DETAIL SUMMARY SHEET

TITLE: The Effects of Simvastatin on Heart Rate Variability in Dilated Cardiomyopathy

KEYWORDS:

PRINCIPAL INVESTIGATOR: Gentlesk, Philip J. CPT MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Cardiology

INITIAL APPROVAL DATE: 16 October 2001

### STUDY OBJECTIVE

The primary objective is to determine if statins (HMG-CoA reductase inhibitors) improve heart rate variability in non-ischemic dilated cardiomyopathy.

### TECHNICAL APPROACH

The study is a 6-week, self-controlled clinical trial evaluating the effects of 20 mg of simvastatin a day on heart rate variability in patients with a non-ischemic dilated cardiomyopathy. Heart rate variability using the ANSAR-R-1000 device is performed at baseline and after a 6-week course of the simvastatin. Baseline lab work to include a hepatic panel, chemistry panel and lipid panel is obtained. The hepatic and lipid panels are repeated at the end of the 6 weeks. No significant changes have been made to the methodology.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been no new literature on statins and heart rate variability, sudden cardiac death or ventricular arrhythmia since submission of the study protocol. Seventeen volunteers have been enrolled in the study. Eleven volunteers have completed the six-week trial. One volunteer was not able to complete the study due to permanent pacemaker placement (unable to perform heart rate variability with pacemaker dependence). No preliminary analysis of the data has been performed. Two unexpected adverse events occurred and have been submitted. Patient study #03 had a permanent pacemaker placed that was not related to the study medication. Patient study #14 had a hospital admission for nonketotic hyperglycemia that was not related to the study medication. Both adverse event reports have been submitted.

The number of subjects enrolled to the study since last APR at WRAMC is 17 and the total enrolled to date at WRAMC is 17.

### CONCLUSIONS

The study appears to be on pace to finish this year. Forty-four percent of the needed sample size of 25 have completed the study. Sixty-eight percent of the needed sample size have been enrolled. There have been no known adverse events related to the study medication. No preliminary analysis of the data is planned. PI plans to perform the data analysis after closure of the study (at least 25 patients have completed enrollment).

## DETAIL SUMMARY SHEET

TITLE: Ventricular Resynchronization Therapy Randomized Trial (VecToR)

KEYWORDS:

PRINCIPAL INVESTIGATOR: Wiley, Thomas LTC MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Cardiology

INITIAL APPROVAL DATE: 29 November 2001

### STUDY OBJECTIVE

The objective of this study is to determine the clinical efficacy of bi-ventricular pacing in patients with intraventricular conduction delay, systolic dysfunction, and congestive heart failure.

### TECHNICAL APPROACH

Patients with the above characteristics will be randomized in a 2:1 ratio to active pacing or no pacing. All patients will undergo placement of a pacing system after collection of baseline data to include six-minute walk test, echo, and cardiopulmonary exercise testing. Patients will then be followed for clinical status and performance on follow-up testing (echo, six minute walk, and exercise testing).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Our final approval letter was only received on 23 October 2002, and we do not have any patients enrolled yet.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is not available.

### CONCLUSIONS

None yet.

## DETAIL SUMMARY SHEET

TITLE: Review of a Humanitarian Device Document

KEYWORDS:

PRINCIPAL INVESTIGATOR: Simpson, Daniel MAJ MC

ASSOCIATES: Dixon, William MAJ MC

DEPARTMENT: Medicine

SERVICE: Cardiology

STATUS: O

INITIAL APPROVAL DATE: 26 March 2002

### STUDY OBJECTIVE

Use of the CardioSEAL septal occluder to percutaneously close Patent Foramen Ovals (PFO) in patients with attributable embolic events as per the Food and Drug Administration's (FDA's) Humanitarian Device Exemption (HDE) program.

### TECHNICAL APPROACH

This is not a research protocol and there have been no modifications to the approach since last year's report dated 4 March 2002. Standard cardiac catheterization technique is performed with the additional utilization of general anesthesia and transesophageal echocardiography for appropriate device placement along the atrial septum.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since last year's report, there have been no significant additions to the percutaneous septal closure literature. There have been three devices implanted in three patients since last year's progress report. An additional device in one patient was percutaneously removed during the initial procedure secondary to inadequate seeding. There were no complications, and there have been no adverse events in follow-up.

### CONCLUSIONS

The undersigned requests a renewal letter from the WRAMC HUC for continued implantation of the CardioSEAL septal occluder in patients with a PFO and attributable embolic events.

## DETAIL SUMMARY SHEET

TITLE: Utility of the Pace-ECG for Diagnosis of Cardiac Hypertrophy

KEYWORDS: electrocardiogram, hypertrophy, cardiomyopathy

PRINCIPAL INVESTIGATOR: Isenbarger, Daniel W., MAJ MC

ASSOCIATES: Duncan, Joan; Taylor, Allen J.

DEPARTMENT: Medicine

SERVICE: Cardiology

STATUS: O

INITIAL APPROVAL DATE: 20 August 2002

### STUDY OBJECTIVE

Correlate ECG findings with echocardiographic measurements of left ventricular mass in patients with RV endocardial pacemakers.

### TECHNICAL APPROACH

Concomitant 12-lead paced ECG and transthoracic echocardiogram are obtained in patients with pacemakers. ECGs are evaluated for QRS voltage, width, axis, and onset of intrinsicoid deflection. Echocardiograms are evaluated for LV septum and posterior wall thickness, then the LV mass is estimated using a mathematical formula that incorporates the LV measurements. ECG findings are evaluated for statistical correlation with LV mass measurements to assess utility of the paced ECG for diagnosis of left ventricular hypertrophy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No amendments to the protocol have been made, and no new research findings impact on the study. No adverse events have occurred, and none are expected. One patient died after consenting to be in the study, but before he could have his echo and ECG obtained. There is no relationship between his death and this study.

The number of subjects enrolled to the study since last APR at WRAMC is 33 and the total enrolled to date at WRAMC is 33. No patients have been withdrawn from the study.

### CONCLUSIONS

Data analysis has not been undertaken, as patient enrollment is still underway. However, it is apparent that enrollment is less than hoped for at this point. Our target enrollment is 100 for the study. We are just 1/3 toward that goal.

## DETAIL SUMMARY SHEET

TITLE: The Accuracy of Physical Examination for the Diagnosis of Aortic Valvular Sclerosis

KEYWORDS:

PRINCIPAL INVESTIGATOR: Sullenberger, Lance, CPT MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Cardiology

STATUS: O  
INITIAL APPROVAL DATE: 27 August 2002

### STUDY OBJECTIVE

The primary objective will be to determine the sensitivity and sensitivity of physical exam as performed by a cardiologist in the diagnosis of aortic sclerosis. The secondary objective will be to determine if the presence of aortic sclerosis, found by physical exam by a cardiologist and/or echocardiography, is a marker of worse outcomes in patients admitted to a coronary care unit in relation to pre-discharge myocardial infarction, need for re-vascularization or death.

### TECHNICAL APPROACH

This study will be a prospective, observational evaluation for aortic sclerosis, with the primary endpoint being to determine the sensitivity of the physical exam by cardiovascular sub-specialists for the presence of aortic sclerosis. All patients over the age of 55 years old who have been admitted to the CCU or the step-down ward will be offered enrollment in the study during their hospital stay. The clinical outcomes that will be assessed at discharge will be myocardial infarction (defined by discharging team of physicians), need for re-vascularization (defined as percutaneous intervention of coronary artery bypass), or death. The only modification made since final approval was the extension of the study patients to the cardiology step-down ward to provide a greater number of patients for recruitment. This modification was approved by the HUC in the spring of 2003.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no significant advances in the literature regarding this particular topic.

The number of subjects enrolled to the study since last APR at WRAMC is 7 and the total enrolled to date at WRAMC is 7.

### CONCLUSIONS

There are not enough data points as yet to draw significant conclusions.  
No adverse events in the past year.

## DETAIL SUMMARY SHEET

**TITLE:** Investigations on  $\gamma$ -Ray-Induced Alterations in Gene Expression Profiles in *wt*-FRTL-5 and Ret/PTC-3 Oncogene Expressing FRTL-5 Thyroid Cell Lines Utilizing cDNA Expression Array

**KEYWORDS:** FRTL-5 cell line, cancer gene, MTT assay, cell survival, ionizing radiation, radiation exposure, cellular RNA, GeneChips, c-DNA expression array, global gene expression profile.

**PRINCIPAL INVESTIGATOR:** Vaishnav, Yashesh N PhD DAC

**ASSOCIATES:** LTC Victor Bernet, M.D., M. C.; COL Henry Burch, M.D., M.C.; Iris Robbins, B.A.; Jeffrey Anderson, M.T.; Matthew Ringel, M.D. and Motoyasu Saji, M.D., Ph.D and Maryanne Vahey, Ph.D.

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Endocrine

**INITIAL APPROVAL DATE:** 13 November 2001

### STUDY OBJECTIVE

1. To determine the  $L_D 50$  for rat FRTL-5 cell line expressing pRC/CMV (normal gene) and RET-PTC-3 (oncogene) after exposure to varying doses of  $^{60}\text{Co}$  (gamma-rays).
2. To identify global changes in the gene expression profiles including several targeted genes (2-5 cellular apoptosis-relevant genes) from both pRC/CMV normal and ret-PTC-3 oncogene expressing FRTL-5 cell lines before and after irradiation (at  $L_D 50$ ) utilizing c-DNA expression array (Affimetrix GeneChip Platform).

### TECHNICAL APPROACH:

Normal (pRC/CMV) and oncogene (RET-PTC3) transformed FRTL-5 cell line seeds are being obtained from our research collaborators (Dr. Ringel et al.) at the Washington Hospital Center, Washington, D.C. These cell lines are being cultured in-house in our Endocrine Research Laboratory at the WRAMC. Once we have sufficient normal and oncogenic cultured cells, we will determine the required optimal/basal cell culture medium condition for the irradiation of cells. Utilizing MTT cell survival and proliferation assay, we will determine the % of survival of both normal and oncogenic cells after a single radiation dose under varying medium composition. The radiation exposure of the cells will be performed at the Armed Forces Radiobiology Research Institute in Bethesda, MD. Once we have determined the optimal cell culture medium condition for the irradiation, we will proceed to determine the  $L_D 50$  (radiation dose at 50% cell survival) for both normal and oncogenic cells in the optimal cell culture medium. After having established the  $L_D 50$  for each cell line, a large number of both normal and oncogenic cells will be exposed to ionizing radiation at the predetermined  $L_D 50$  radiation dose. Once the cells are irradiated, we will extract total RNA from each category of irradiated and nonirradiated control cells. Once we have the total RNA from the cells available, Dr Vahey's research group (our research collaborator, Walter Reed Army Institute of Research) will process RNA samples for the GeneChip and, develop and scan the GeneChips, assuring the quality and integrity of all GeneChip experiments. Dr. Vahey will provide us the primary data for the subsequent analysis.

### Minor Modifications in the Protocol:

- (a) In our original version of the protocol we had proposed to use a clonogenic assay to study cell survival and proliferation after radiation exposure; however, we have been utilizing 'MTT Assay' for the cell survival study because MTT assay has been reported to be equally good and less time consuming.
- (b) We have been utilizing an FRTL-5 cell line containing pRC/CMV insert as our normal cell model, rather than the *wt*-FRTL-5 cell line because the former cell line will serve better.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE:

We have received seed cells containing pRC/CMV and RET-PTC inserts in FRTL-5 cell line from Dr Ringel's research group (WHC). From these seed cells, we have cultured sufficient numbers of both normal and oncogenic FRTL-5 cells in-house successfully. Currently, we have been testing the MTT assay procedures on these cell lines to determine their feasibility for cell survival studies. We are now ready for the next phase of our research - radiation exposure of the normal and oncogenic FRTL-5 cell lines.

The number of subjects enrolled to the study since last APR at WRAMC is: N. A., and the total enrolled to date at WRAMC is N. A.

Amendment or modifications to research study: Minor modifications in the study are made and have been shown in the Technical Approach section.

Adverse events (A.E.) expected and/or serious for WRAMC site: None

A.E. for other sites if multi-center study: None

CONCLUSIONS

We have successfully cultured sufficient numbers of both normal and oncogenic FRTL-5 cell lines to proceed to the radiation exposure phase of this protocol.

## DETAIL SUMMARY SHEET

**TITLE:** The Use of Heart Rate Variation to Determine the Prevalence and Prognostic Significance of Autonomic Neuropathy in Patients with Either Diabetes Mellitus or Cardiovascular Disease

**PRINCIPAL INVESTIGATOR:** Vigersky, Robert A., COL MC

**DEPARTMENT:** Medicine  
**SERVICE:** Endocrine

**STATUS:** O  
**INITIAL APPROVAL DATE:** 26 February 2003

### STUDY OBJECTIVE

This is a prospective, observational study to detect autonomic neuropathy in either patients with diabetes or cardiovascular disease as it may represent a significant risk factor for morbidity and mortality. There are eight major objectives for this study – four each for the diabetes and cardiovascular components.

#### Objectives for Diabetes Mellitus Component:

Determine the prevalence of Diabetic Autonomic Neuropathy (DAN) in the military diabetic population  
Describe the cross-sectional relationships between DAN and stress echocardiography and other cardiovascular risk markers.  
Describe the relationship between DAN and cardiovascular outcomes.  
Explore the relationship between measures of glycemic control and changes in DAN.

#### Objectives for Cardiovascular Disease Component:

Determine the prevalence of abnormal HRV in patients with known cardiovascular disease.  
Determine the cross-sectional relationships between HRV and other risk variables in chronic ischemic heart disease.  
Evaluate the prognostic significance of HRV testing in patients with established cardiovascular disease.  
Assess the efficacy of autonomic neuropathy testing in early detection of atherosclerosis burden.

All eligible patients with Diabetes Mellitus will undergo autonomic neuropathy testing using the ANSAR ANS-R-1000 at the time of their routine visit to their provider. All eligible cardiovascular service patients with or without known cardiovascular disease will undergo autonomic neuropathy testing at the time of their routine visit to their provider (outpatients) or prior to hospital discharge (inpatients). All patients will receive the standard of care for their condition.

### TECHNICAL APPROACH

The ANSAR ANS-R-1000 measures heart rate variability in real time during inspiration and expiration, during a Valsalva maneuver, and during a change in posture from sitting to standing. It is comprised of a standard computer to which are attached EKG leads and two peripheral devices: a non-invasive blood pressure monitor, and an apnea monitor. The blood pressure monitor takes readings when manually activated by the operator. The apnea monitor records both heart rate and respiratory rate. By simultaneously analyzing the spectral content of both the EKG and the respiratory signals through real time fast Fourier transformation, the software is able to determine the activity level of both the parasympathetic and sympathetic nervous system. The HRV response to deep breathing is indicative of the tone of the parasympathetic nervous system (PSNS). The Valsalva maneuver is a sympathetic nervous system (SNS) challenge. The Stand challenge is a combined SNS and PSNS challenge. The SNS is challenged during the first couple of minutes of the Stand challenge as a result of gravity affecting the cardiac hydrostatic column while the PSNS is challenged during the final few minutes to support the change.



PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since approval of the protocol, numerous milestones have been reached.

1. Hired, trained, and deployed the following personnel: 1 project officer, 1 ultrasound technician, and 5 ANSAR technicians.
2. The ANSAR R-1000 instruments have been safety inspected and two instruments have been deployed to each of the following MTFs: KACC, DACH, Woodbridge Clinic, Fairfax Clinic, Rader Clinic, WRAMC Endocrine Clinic, WRAMC Cardiology Clinic
3. BP cuffs, stethoscopes, a computer, phone lines, and office furniture have been purchased in support of the protocol
4. Space in each of the above clinics has been dedicated to patient testing, which includes adequate space for the instrument and technician
5. Patient recruitment has begun through the nurse practitioners of the Diabetes Institute and the WRAMC Cardiology Clinic

The following changes were made in the protocol in request made on 17 December 2002:

1. Increase the number of subjects in Objective 2 from 200 to “up to 250” in order to be certain that 200 interpretable studies will be obtained, since there may be up to 25% of the studies that may be uninterpretable due to technical considerations (e.g. limited view of the cardiac silhouette due to obesity, inability to achieve the target heart rate, etc.).
2. Add a Carotid Intimal Medial Thickness study at 12, 24, and 36 months in the “up to 250” patients in Objective 2. This will permit more complete assessment of the potential value of autonomic neuropathy testing allowing correlations with other non-invasive markers done at the same time points.
3. Modification of the Diabetes Consent form to reflect the changes in the number of Carotid Intimal Medial Thickness tests and the number of patients that will have the CIMT and stress echocardiograms.
4. The recruiting techniques have been expanded to include a tri-fold brochure and a flyer to be e-mailed.

The only modification to the protocol has been the recruitment flyer and patient information tri-fold brochure. There have been no serious adverse events.

The number of subjects enrolled to the study since last APR at WRAMC is 66 and the total enrolled to date at WRAMC is 66.

CONCLUSIONS

All the elements for conducting the study are in place and accession of subjects is going smoothly. It is too early for any data analysis.

## DETAIL SUMMARY SHEET

TITLE: Effect of a Single Intra-Articular Steroid Injection on Serum Glucose Levels in Patients with Type 2 Diabetes Mellitus

KEYWORDS:

PRINCIPAL INVESTIGATOR: Gaitonde, David Y. CPT MC

ASSOCIATES: McKinley, Brian T. CPT MC

DEPARTMENT: Medicine

SERVICE: Endocrine

STATUS: O

INITIAL APPROVAL DATE: 12 March 2002

### STUDY OBJECTIVE

To investigate the effect that a single injection of intra-articular steroids has on the blood sugar levels of patients with type 2 diabetes.

### TECHNICAL APPROACH

Patients are enrolled through the Rheumatology or Endocrine clinics. All patients identified as candidates for a steroid injection into the knee receive the steroid injection regardless of whether they elect to enroll in the study. Patients who wish to participate in the study are then instructed on the schedule of blood draws and on how to record their home monitored blood glucoses (HMBG). Patients are asked to go to the lab three times: the day of the injection; 2 weeks after the injection; and 4 weeks after the injection. Patients are asked to mail, fax, or personally drop off their record of HMBG. Finally, patients are asked to rate their activity level during the four weeks following the steroid injection.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No new literature is available.

Too few patients have been enrolled for adequate review and analysis of data.

There are no amendments or modifications.

A total of four patients have been enrolled.

There have been no adverse events.

No patients withdrew from the study. However, one patient did not complete the study because she was unable to return from a trip in time to have the 4-week labs drawn.

The number of subjects enrolled to the study since last APR at WRAMC is 4 and the total enrolled to date at WRAMC is 4.

### CONCLUSIONS

Active enrollment is ongoing. Given the limited number of patients enrolled to date no analysis of data has been performed.

## DETAIL SUMMARY SHEET

TITLE: An Assessment of Ocular Lens Fluorescence Measurements for the Detection of Diabetes: A Joint Joslin Diabetes Center, Tripler Army Medical Center, and Walter Reed Army Medical Center Protocol

KEYWORDS:

PRINCIPAL INVESTIGATOR: COL Robert A. Vigersky MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Endocrine

STATUS: O  
INITIAL APPROVAL DATE: 23 April 2002

STUDY OBJECTIVE

To evaluate a methodology that uses ocular lens fluorescence for the early, non-invasive detection of Type 2 Diabetes Mellitus in previously undiagnosed subjects.

TECHNICAL APPROACH

This is an observational, prospective study to determine the accuracy of an investigational instrument, the Accu-Chek D-Tector, in screening for previously undiagnosed Diabetes Mellitus.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been no work on this protocol. Roche has withdrawn the instruments from all investigators (we never received one) because there are legal issues. They have stated to me that there are no safety issues involved in this recall. If and when the instrument becomes available, patient recruitment will begin. The LXN Corporation, (the maker of the In-Charge Diabetes Control System Monitor), was purchased by Inverness Medical Technologies last year and has ceased making the In-Charge Monitor. If we gain access to the Accu-Chek D-Tector, then an amendment to the protocol will be filed to eliminate the use of this meter.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

CONCLUSIONS

Work on the protocol never began and is currently in limbo until Roche permits use of their technology.

Report Date: 1 May 2003

Work Unit # 02-13010

## DETAIL SUMMARY SHEET

TITLE: Home Fructosamine Testing As A Cost-Effective Adjunctive Tool For Improving Glucose Control In Inadequately Controlled Type 2 Diabetes Mellitus

KEYWORDS:

PRINCIPAL INVESTIGATOR: Glistner, Babette C., CPT MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Endocrine

STATUS: W  
INITIAL APPROVAL DATE: 28 May 2002

### STUDY OBJECTIVE

Study withdrawn.

### TECHNICAL APPROACH

Study withdrawn.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn.

### CONCLUSIONS

Study withdrawn.

## DETAIL SUMMARY SHEET

TITLE: The Effects of Variations in Diet Composition on Body Mass

PRINCIPAL INVESTIGATOR: Glister, Babette C., CPT MC

ASSOCIATES: Bernet, Victor J., LTC, MC; Stocker, Derek J., MAJ, MC; Parham, Diana, LTC, MC; Goldberg, Robert B., RD, LD (civilian)

DEPARTMENT: Medicine

STATUS: O

SERVICE: Endocrine

INITIAL APPROVAL DATE: 6 August 2002

### STUDY OBJECTIVE

To evaluate the effects of a traditional low calorie diet versus a low carbohydrate, low calorie diet on body mass index and composition.

### TECHNICAL APPROACH

This is a prospective randomized clinical trial comparing a low carbohydrate diet, consisting of 30 to 40 grams of carbohydrates per day, with a traditional low calorie diet. Obese patients will be stratified by baseline percent body fat (25-30%, 31% to 40%, >40%) and randomized to diet with an equal number of subjects in each diet group. Randomization will be determined using a computer program based on random number generation.

Initial screening and recruitment will be used for the aforementioned inclusion and exclusion criteria. Baseline lab values (including fasting chemistries, associated liver enzymes, fasting lipid panel, fasting insulin level, urinalysis, thyroid function panel and 24-hour urine collection for creatinine, calcium, and sodium) will be obtained for each subject. In addition, subjects will have a baseline EKG completed prior to beginning the study. All female patients will have a urine pregnancy test at the onset of the study as well as every 4 weeks or whenever pregnancy is suspected, since continued dieting could be detrimental to a developing fetus and thus pregnancy would preclude the subject from progressing further in the protocol. A baseline Dual X-Ray Absorptiometry (DEXA) will be completed on each patient to establish body mass composition. Subject research files will include age, date of birth, sex, height, weight, body mass index, blood pressure (BP), pulse, waist circumference, hip circumference and waist to hip ratio (WHR). The person conducting the DEXA and those persons measuring subjects' height, weight, blood pressure, pulse, waist circumference, and hip circumference will be blinded to the patient's diet assignment. Confidentiality will be maintained in all records.

All subjects will attend a one-hour group introduction class that will be conducted by a registered dietician under the direction of CPT Macmillan at the WRAMC Wellness Center, where they will learn about diet exchanges and the food pyramid adapted from the U.S. Department of Agriculture and the U.S. Department of Health and Human Services. They will be randomized to the low calorie vs. low carbohydrate/low calorie diet prior to this to allow them to attend the appropriately focused class. Subjects will receive instructions on their individual diet composition (either low carbohydrate/low calorie or low calorie alone) and be given food diaries to record their food intake. Each subject will receive a diet exchange handout and specific instructions on how to complete their food diary and comply with their specific diet plan, with the chance to have all questions answered regarding this as part of the group session. Diet composition will consist of a standard diet of 15% protein, 20-30% fat, and 55-60% carbohydrate with total calories determined for each individual by estimating basal energy expenditure (BEE) [using the Harris-Benedict equation for males:  $66 + 13.8 (\text{weight in kg}) + 5 (\text{height in cm}) - 6.8 (\text{age in yr})$  and for females:  $655 + 9.6(\text{weight in kg}) + 1.8 (\text{height in cm}) - 4.7 (\text{age in yr})$ ], multiplying BEE by an activity factor of 1.1, 1.2, or 1.3 and subtracting 500 calories for a planned weight loss of one pound per week. The activity factor is determined based on patients' usual activity level, 1.1 for sedentary, 1.2 for light exercise and 1.3 for strenuous exercise. Alternatively, the low carbohydrate, low calorie diet will consist of an initial 20-40 grams of carbohydrate per day with calories limited to 500 kcal below calculated needs (the "induction phase"), followed

by conversion to a less intensive “maintenance phase” with 50-70 grams of carbohydrate per day after the initial two months of the study period (with continuation of the low calorie diet as stated above).

All subjects will also attend a second one-hour group class by Mr. Robert Goldberg at the WRAMC Wellness Center introducing them to the importance of exercise and the benefits of being consistent with an exercise program. They will then be given instructions on exercise and followed by Mr. Goldberg for the duration of the study. Each subject will receive a subsequent one-hour fitness analysis consisting of height, weight, BMI, flexibility, strength, and endurance and will be given a program for exercise. Subject flexibility will be measured and recorded using Trifit. Trifit is a standardized and validated machine that measures flexibility while a patient sits on it, like a bicycle. Strength will also be measured by the Trifit machine using bicep curls. Subject endurance will be measured as VO2 max using the Monarch exercycle. Weekly visits to the Wellness Center will be mandatory for all subjects during the study period to have their height, weight, BP, pulse measured and their BMI calculated. These visits will be run by representatives of the Wellness Center under the direction of LTC Rowbotham, Director of Wellness Services. A subject will be excluded from continuing in the study if more than three consecutive visits *or* four total visits are missed. Subjects will be assigned a unique study identification code at the onset of the study. This subject study ID code will not include any specific personal identifiers such as social security number, name, or medical record number. A master list that links subjects' personal information with their study ID codes will be kept in a locked file cabinet in a locked room within the WRAMC Endocrinology clinic. Only the principal investigator and associate investigators will have access to the file cabinet containing this sensitive information. This master file will be maintained for up to 3 years after study completion to allow for analysis and publication of the data.

Note: No modifications have been made to the methodology since the protocol was approved in April 2003.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Within the last four months, the literature on low carbohydrate and high protein diets has increased dramatically. This is a reflection of the great deal of interest that the general public and the medical community have placed in this novel diet concept. In April 2003, JAMA published a systematic review of the literature on low carbohydrate diets by Bravata and colleagues, which concluded that significant weight loss occurred without noticeable adverse effects on lipids, glucose metabolism, or blood pressure, but that the loss was probably actually due to caloric restriction that anything specific to carbohydrate content. The New England Journal of Medicine then published two separate articles in May 2003. Both suggested that a small but significant weight loss advantage was seen in the low-carbohydrate vs. conventional low calorie diet groups, which was associated with associated improvement in some metabolic parameters, though less significantly so by 12 months compared to 6 months. The only recent study looking at body composition as a measure of benefit in low-carbohydrate dieting is by Brehm et al. in the April 2003 issue of the Journal of Clinical Endocrinology and Metabolism. This study randomized healthy women with body mass indices of 30-35 to a very low-carbohydrate (15% carbohydrate) vs. conventional low-calorie diet for 6 months. They found that both total fat mass and lean body mass decreased significantly in the low-carbohydrate group compared to the low-calorie group, with 50-60% of the overall weight loss attributable to fat mass loss.

In our study, we would like to look at this further in both men and women, as well as in subjects with varying degrees of obesity, to confirm and better characterize the findings of this last study. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

#### CONCLUSIONS

No conclusions can be made to date since the protocol has not begun enrolling subjects to date.

## DETAIL SUMMARY SHEET

TITLE: Continuous Glucose Monitoring in Patients With Type 2 Diabetes Mellitus

PRINCIPAL INVESTIGATOR: Vigersky, Robert A., COL MC

ASSOCIATES: Jehanara Ahmed, M.D.

DEPARTMENT: Medicine

STATUS: O

SERVICE: Endocrine

INITIAL APPROVAL DATE: 17 September 2002

### STUDY OBJECTIVE

The management of blood glucose in diabetes is based primarily on patients monitoring their own blood glucose levels. With the advancement of technology, it is now possible to continuously monitor blood glucose. Our objective is to take advantage of this technology and to use it to improve the glycemic control in Type 2 diabetics. This will give us the opportunity to evaluate the glycemic excursions and trends that are not easily available with periodic blood glucose meter readings. The knowledge of these trends in fluctuation of blood glucose may be used to make appropriate changes in diabetic management. It will also determine when a finger stick test most accurately reflects overall glycemic control. We believe that with continuous blood glucose monitoring, we will obtain valuable information necessary to make recommendations that can significantly improve patients' glycemic control and reduce the risk of long-term complications. Another advantage of continuous monitoring is to detect hypoglycemia, a major complication of intensive glucose control, and manage it appropriately.

### TECHNICAL APPROACH

No modifications have been made. The MiniMed Continuous Glucose Monitoring System is a Holter style sensor system that continuously automatically monitors glucose values in subcutaneous tissue fluid. It has four primary components:

1. Continuous glucose monitor - a pager-sized device.
2. Cable that provides transmission of signals from glucose sensor to the monitor.
3. Glucose sensor is an electrode containing the enzyme glucose oxidase. It is inserted just under the skin (usually in the abdominal area) and secured with a dressing.
4. Com-Station, a data downlink communication station that enables data to be sent into a personal computer.

The Accu-Chek Advantage meter is the standard meter used in the Walter Reed Health Care System.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The study began to recruit in February 2003 after training had been obtained on the use of the CGMS apparatus. Since that time, approximately 100 patients have been screened for this study. Only 6 have been found to be eligible due to the strict exclusion criteria and necessity for frequent visits. Of the 6, 4 refused once the protocol was explained to them in detail. Of the 2, one dropped out after the first CGMS period and the other does not appear to have benefited from the use of the technology based on their post-CGMS insulin modification.

The Associate Investigator and Research Project Officer, Dr. Jehanara Ahmed, has been accepted into an Endocrinology Fellowship at Howard University and will no longer be participating in this study as of September 2003.

The number of subjects enrolled to the study since last APR at WRAMC is 2 and the total enrolled to date at WRAMC is 2.

### CONCLUSIONS

Recruiting problems have prevented accrual of patients for this study. This study has not been assigned to a new Fellow or Project Officer.

## DETAIL SUMMARY SHEET

TITLE: The Role of Gastroesophageal Reflux Disease (GERD) in Upper Airway Reactivity Syndrome

PRINCIPAL INVESTIGATOR: Mulhall, Brian P., CPT MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Gastroenterology

INITIAL APPROVAL DATE: 16 October 2001

### STUDY OBJECTIVE

- 1) Evaluate the prevalence of Gastroesophageal Reflux Disease (GERD) in patients with Upper Airway Resistance Syndrome (UARS).
- 2) Define any temporal relationship between arousals in UARS and GERD events (as determined during polysomnographic monitoring protocol).
- 3) Explore the association of demographic or clinical variables with the prevalence and severity of GERD, the frequency of arousals, and the GER/arousal index for this population.
- 4) If a high prevalence of GERD is discovered, then to prospectively evaluate the effect of GER therapy on the sleep pattern/efficacy in a group of patients with UARS. Ten to fifteen patients who are being appropriately treated with a proton-pump inhibitor (with the goal of decreasing efforts on the esophagus) will undergo a repeat sleep study to assess for any improvement in their arousal pattern.

### TECHNICAL APPROACH

Phase I: Consecutive patients referred to the Sleep Disorder Center for evaluation of Sleep Disorders (specifically assessing for UARS) have been provided information regarding this study. Interested patients have provided informed consent just prior to their polysomnograph/sleep study. Patients have then completed questionnaires – covering some demographic data and including the Epworth Sleep Scale (standard of care) and the Gastroesophageal Reflux Symptom Scale (research) – and have then undergone their Sleep Study according to the established protocol of the Sleep Disorders Center of the Walter Reed Pulmonary Clinic (standard of care). Sleep study protocol entails placement of an esophageal pressure monitor probe (placed nasally), placement of EKG probe, two EOG (electro-oculography) probes, two EEG (electroencephalogram) probes, and three EMG (electromyogram) probes on the chin and legs, respectively. Additionally, a pressure flow transducer is placed at the nares. (All standard of care.) This protocol has entailed the placement of a small nasoesophageal pH probe (2 mm in diameter) placed side-by-side with esophageal pressure catheter. (Research). By report of the several enrolled patients so far, the nasal intubation with the pH probe has not significantly changed the overall experience of the sleep study. At completion of the sleep study, subjects have all apparatuses removed and are released. All data is being collected in paper format, at present, and will be entered and analyzed en bloc after each series of ten patients has been enrolled.

Phase II: Phase II has not yet begun. If the prevalence of GERDs in the UARSs population is well defined, we will proceed to Phase II and include updates in the APR.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no new or significant publications regarding the relationship between UARS and gastroesophageal reflux since the initiation of this protocol. We will have preliminary data over the next several weeks. There have been no adverse events. Two patients will not be included in our first data analysis, as the pH probes failed to obtain readings throughout the night.

The number of subjects enrolled to the study since last APR at WRAMC is 9 and the total enrolled to date at WRAMC is 9.



CONCLUSIONS

Patient enrollment has been slower than anticipated due to fewer scheduled patients (that have met inclusion criteria) than previously anticipated. Only two patients have failed to consent to enrollment of the eleven provided information regarding the study. Two patients have uninterpretable data due to equipment failure, but these technical problems should be uncommon in the future due to the use of newer pH catheters (same model, newly purchased). Initial data analysis will take place after another three patients are enrolled, and preliminary data will be reviewed by all investigators to gauge the need for any modifications to the present approach. Overall, there are no obvious problems, anticipated changes, or clear conclusions at this time. There is no new published data to impact our present approach. However, the protocol is progressing, and we anticipate completion of data collection within the next year, with or without a Phase II.

## DETAIL SUMMARY SHEET

TITLE: The Effect of Interferon Therapy on Hearing in Adult Patients with Chronic Hepatitis C

PRINCIPAL INVESTIGATOR: Mulhall, Brian P., CPT MC

ASSOCIATES: Kent Holtzmuller, MD; David Chandler, PhD; Gerald Schuchman, PhD; Pia Cassarino-Leppler, RN; Julia Friend, PA

DEPARTMENT: Medicine

STATUS: O

SERVICE: Gastroenterology

INITIAL APPROVAL DATE: 16 October 2001

### STUDY OBJECTIVE

The purpose of this protocol is to evaluate the effects of interferon therapy on hearing. As such, we are examining the incidence of hearing loss in patients with Hepatitis C undergoing therapy with interferon. We are specifically looking at the timing of onset, severity, and reversibility if and when hearing loss is detected. Additionally, we hope to compare the differences between incidence of, and the character of, hearing loss during therapy with regular interferon versus pegylated interferon if any hearing loss is detected in these two populations of patients.

### TECHNICAL APPROACH

Consecutive patients referred to the Hepatology Clinic (of the Gastroenterology Service at Walter Reed) with chronic hepatitis C have been informed about this study. Patients who meet indications for interferon therapy (and are enrolled in one of the three ongoing treatment protocols) provide informed consent and are enrolled. They obtain interferon and are instructed on the anticipated monitoring regimen defined in our individual interferon protocols. Patients then have an initial audiometric assessment using standard audiometry and Otoacoustic Emissions (OAEs) within 72 hours of enrollment (and prior to starting interferon therapy). Thereafter, the patients have had repeated OAEs at three-month intervals which will continue until completion of the interferon therapy. The length of the interferon therapy may vary from three months up to one year, according to the patient's response. If the patient's hearing has been abnormal before taking interferon, but we are still able to use standard Audiometry and DPOAEs to measure their hearing level, then the patient is still offered enrollment. However, if the patient's hearing level were required for accurate assessment (generally patients with hearing below 30 Dbl.s have inaccurate DPOAEs), they would generally not be enrolled in this study. This has yet to occur. If a patient's hearing changes during the study to the degree that we can no longer accurately measure the amount of hearing loss (again, usually less than 30 Dbl.s with DPOAEs), then the patient could be disenrolled from this study. But, again, this has not yet occurred in the protocol thus far. If at any point a particular patient's hearing worsens by >25%, they will be scheduled for a repeat assessment by both standard audiometry and DPOAE. The patient would then undergo closer follow-up (as directed by the hearing specialist) – likely repeat assessments every four to six weeks. If dramatic hearing loss (>45% over three hearing tests) occurs, then we will strongly consider discontinuing the interferon. But, Dr. Holtzmuller will make the final decision after carefully analyzing the case/indication and discussing the risks and benefits of continuing or discontinuing the medication with the patient. If we find any change in the patient's hearing, and it has not resolved at six weeks status post interferon completion, then we will repeat the hearing studies (both audiometry and DPOAEs) one last time as part of this protocol at six months after completion of therapy. If, at any point in the study, patients are found to have persistent changes in their hearing, they will be referred to the Audiologist for continued follow-up, monitoring, and therapy as appropriate.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been no new literature exploring the relationship between interferon therapies and hearing loss since the initiation of this protocol. There have been no amendments to the protocol, changes to the consent form, or adverse events. Data collection is still in the early phases, as changes are likely to be subtle and may occur later in therapy. Given that the first patient was enrolled seven months ago, no patients have completed the entire 48 weeks of a treatment protocol for final data analysis. However, one study participant was discontinued from

interferon therapy at the 24<sup>th</sup> week, and his final follow-up hearing study will be completed in the next four weeks. (He had no noted hearing loss during the period of observation.) Only one patient was lost from this protocol, due to discontinuation of interferon therapy (due to other, typical side effects of interferon). Early assessments have shown only mild (<10%) changes in the hearing parameters for two of the seventeen patients enrolled to date. Only one patient has completed their hearing studies through the sixth month of treatment. Three will have their 24<sup>th</sup> week studies in the next four weeks. Again, there have been no adverse events, and no withdrawals from the study.

The number of subjects enrolled to the study since last APR at WRAMC is 17 and the total enrolled to date at WRAMC is 17.

#### CONCLUSIONS

Data collection is still in the early phases. We expected that any hearing loss or changes in hearing parameters might be subtle and might be more likely to be noticed later in the treatment regimen. As such, preliminary data suggests no new findings contrary to these expectations and offer no reason to alter the protocol at this time. Once at least five patients have reached the six-month (or 24-week) hearing assessment, we will do preliminary analysis to evaluate for any evidence for a pattern of change. We anticipate continued enrollment of subjects throughout the next year with continued follow-up of all individuals enrolled.

## DETAIL SUMMARY SHEET

TITLE: The Clinical Impact of Gastroesophageal Reflux in Adult Patients with Obstructive Sleep Apnea

KEYWORDS: Gastroesophageal reflux, Obstructive Sleep Apnea Syndrome, Barrett's esophagus, Nexium  
PRINCIPAL INVESTIGATOR: Mulhall, Brian P. CPT MC

ASSOCIATES: Roy KH Wong, MD; David Kristo, MD; Teotimo Andrada, Corrine Maydonovitch

DEPARTMENT: Medicine  
SERVICE: Gastroenterology

STATUS: O  
INITIAL APPROVAL DATE: 26 March 2002

### STUDY OBJECTIVE

To establish the prevalence of gastroesophageal reflux in Obstructive Sleep Apnea Syndrome and its relationship (temporally) to apneas/arousals; to determine the prevalence of Barrett's in this population; and to assess for any effects of anti-reflux medications on sleep quality outcomes in patients with Obstructive Sleep Apnea Syndrome.

### TECHNICAL APPROACH

No modifications to date.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Enrollment will begin in February 2003. Technical difficulties with our manometry equipment has delayed enrollment, but we expect to enroll 1-2 persons per day starting in the second of third week of February 2003. One recent article confirmed the high incidence of gastroesophageal reflux in the Obstructive Sleep Apnea Syndrome population.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

We look forward to patient enrollment in the upcoming weeks.

## DETAIL SUMMARY SHEET

TITLE: A Multicenter, Double-Blind, Three-Way Crossover Intraesophageal and Intragastric pH Study of Three Esomeprazole Treatment Regimens in Documented Barrett's Esophagus Patients

KEYWORDS:

PRINCIPAL INVESTIGATOR: Wong, Roy K.H. COL MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Gastroenterology

INITIAL APPROVAL DATE: 26 March 2002

### STUDY OBJECTIVE

#### A. Primary

The primary objective of this study is to compare the total percent of time during the 24-hour monitoring period that gastric pH is above 4.0 at steady-state (Day 5) in patients with documented Barrett's esophagus when they are taking: esomeprazole 40 mg bid or esomeprazole 40 mg tid or esomeprazole 20 mg tid.

#### B. Secondary

The secondary objectives will compare the total percent time distal esophageal pH is above 4.0 at steady-state for each treatment period. Also, a comparison will be made of the total percent time distal esophageal and gastric pH are above  $x$  (where  $x = 3, 3.5, 4.5, 5, 5.5$  and  $6$ ) at steady-state of each treatment period.

### TECHNICAL APPROACH

At the GI clinic at WRAMC patients with known long segment Barrett's after agreeing to participate in the study will have a series of visits.

1. Visit #1 will consist of a baseline 24-hour PH dual probe. LES (Lower Esophageal Sphincter) location may be obtained at the time of the study or may be obtained from previous examinations in the clinic if available.
2. Patients will then be randomized to the first of three doses of nexium
  - a. Esomeprazole 40 mg bid
  - b. Esomeprazole 40 mg tid
  - c. Esomeprazole 20 mg tid
3. On day 5 of the dosing schedule assigned the patient will present for the second 24-hour PH. During the proceeding 4 days they will be given Gelusil tablets for rescue acid suppression if needed.
4. Once the first regimen is completed there will be a 10-14 day washout period. During this washout period the patients will be allowed to take Gelusil tablets for acid suppression as needed. Following the washout period they will present for the second of three dosing regimens.
5. On day # 5 of the second dosing regimen the patient will present to the GI clinic again for the third 24-hour PH probe. This will be followed by a 10-14 day washout period. At the end of the washout period the patient will present for the 3<sup>rd</sup> dosing regimen. On day 5 of the third dosing regimen the patient will come in for the last 24-hour PH probe.

Each patient will complete a diary of the times the study medication and meals were taken on the days of the pH studies.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 3 and the total enrolled to date at WRAMC is 3. The total number enrolled study-wide is 27, if multi-site study. There have been no adverse events at WRAMC site however there are a total of 25 events that have been reported from all sites. These events do not increase the risk of this study.

### CONCLUSIONS

There are no conclusions at this time.

## DETAIL SUMMARY SHEET

TITLE: A Multicenter, Double-Blind, Three-Way Crossover Intraesophageal and Intragastric pH Study of Three Esomeprazole Treatment Regimens in Documented Barrett's Esophagus Patients

KEYWORDS:

PRINCIPAL INVESTIGATOR: Wong, Roy K.H. COL MC

DEPARTMENT: Medicine

STATUS: C

SERVICE: Gastroenterology

INITIAL APPROVAL DATE: 26 March 2002

### STUDY OBJECTIVE

#### A. Primary

The primary objective of this study is to compare the total percent of time during the 24-hour monitoring period that gastric pH is above 4.0 at steady-state (Day 5) in patients with documented Barrett's esophagus when they are taking: esomeprazole 40 mg bid or esomeprazole 40 mg tid or esomeprazole 20 mg tid.

#### B. Secondary

The secondary objectives will compare the total percent time distal esophageal pH is above 4.0 at steady-state for each treatment period. Also, a comparison will be made of the total percent time distal esophageal and gastric pH are above  $x$  (where  $x = 3, 3.5, 4.5, 5, 5.5$  and  $6$ ) at steady-state of each treatment period.

### TECHNICAL APPROACH

At the GI clinic at WRAMC patients with known long segment Barrett's after agreeing to participate in the study will have a series of visits.

1. Visit #1 will consist of a baseline 24-hour PH dual probe. LES (Lower Esophageal Sphincter) location may be obtained at the time of the study or may be obtained from previous examinations in the clinic if available.
2. Patients will then be randomized to the first of three doses of nexium
  - a. Esomeprazole 40 mg bid
  - b. Esomeprazole 40 mg tid
  - c. Esomeprazole 20 mg tid
3. On day 5 of the dosing schedule assigned the patient will present for the second 24-hour PH. During the proceeding 4 days they will be given Gelusil tablets for rescue acid suppression if needed.
4. Once the first regimen is completed there will be a 10-14 day washout period. During this washout period the patients will be allowed to take Gelusil tablets for acid suppression as needed. Following the washout period they will present for the second of three dosing regimens.
5. On day # 5 of the second dosing regimen the patient will present to the GI clinic again for the third 24-hour PH probe. This will be followed by a 10-14 day washout period. At the end of the washout period the patient will present for the 3<sup>rd</sup> dosing regimen. On day 5 of the third dosing regimen the patient will come in for the last 24-hour PH probe.

Each patient will complete a diary of the times the study medication and meals were taken on the days of the pH studies.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 3. The total number enrolled study-wide is 27, if multi-site study. There have been no adverse events at WRAMC site. However, there are a total of 12 events that have been reported from all sites. These events do not increase the risk of this study.

### CONCLUSIONS

There are no conclusions at this time.

## DETAIL SUMMARY SHEET

**TITLE:** The Effect of Baclofen on Patients with Gastroesophageal Reflux and Normal Lower Esophageal Sphincter Pressures: A Randomized Prospective Study

**KEYWORDS:** Baclofen, GERD

**PRINCIPAL INVESTIGATOR:** Mark Cossentino, MAJ, MC

**ASSOCIATES:** Corinne Maydonovitch, Lavern Bell, Roy Wong, COL, MC

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Gastroenterology

**INITIAL APPROVAL DATE:** 23 April 2002

### STUDY OBJECTIVE:

To determine the effect of the pharmacological agent baclofen in patients with gastroesophageal reflux disease (GERD), as measured by 24-hour pH monitor (% time pH<4, Johnson-Demeester score) and clinical symptom score. This study is only being performed at WRAMC, ie, single center study.

### TECHNICAL APPROACH

The technical approach includes performing an esophageal manometry and 24-hour pH probe on patients with GERD at baseline and then after two weeks of either baclofen or placebo. This study is less than a year old and the design has not changed except for the fact that when we began, we only enrolled patients with normal lower esophageal sphincter pressures (LESP). Since then another publication has shown that baclofen may also decrease GERD in patients with low LESP. (See below.)

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

After reviewing the article *Control of transient lower oesophageal sphincter relaxations and reflux by the GABA (B) agonist baclofen in patients with gastro-oesophageal reflux disease* by Zhang and colleagues (1) we decided to allow patients with low LESP to enter our study. This served two purposes. First we would be able to enroll more patients for our study and second, we would be able to study the effects of baclofen on another population of GERD patients. In November 2002, we submitted an addendum to this effect which was approved by DCI. This did not alter the design of the study or increase the risk of the study.

Since we started recruiting patients in May 2002, we have enrolled a total of 16 patients. One patient changed jobs and moved from the area so he quit the study after he signed the consent form but prior to taking any medications. Another patient with a history of recurrent headaches complained of a headache so she stopped her study medication. When we spoke with the patient she had already discontinued her study medications 3 days prior and did not wish to continue. A third patient complained of a headache and some nausea and discontinued her medications after one day of symptoms. She felt better the next day but did not wish to continue in the study. Both headache and nausea are possible side effects and this is stated clearly in the consent form. No permanent symptoms were noted and none of these patients required office visits or hospitalizations. There were no serious side effects noted. The other twelve patients completed the study without complaints or problems. One patient (Patient #16) is taking study medications now and will complete study on March 18.

The number of subjects enrolled to the study since last APR at WRAMC is 16 and the total enrolled to date at WRAMC is 16.

### CONCLUSIONS

Study is ongoing. Preliminary data shows a trend for decreasing reflux with study medications. However at this time there are no statistically significant results.

## DETAIL SUMMARY SHEET

TITLE: Use of a Hyperspectral Imaging System for Dysplasia Screening in Patients with Long Spectrum Barrett's Esophagus – A Pilot Study

KEYWORDS:

PRINCIPAL INVESTIGATOR: Duncan, Marten CPT MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Gastroenterology

STATUS: O  
INITIAL APPROVAL DATE: 28 May 2002

### STUDY OBJECTIVE:

Evaluate a novel endoscopic imaging modality.

### TECHNICAL APPROACH

Patients undergo an upper endoscopy. During the exam an image and biopsy are obtained in the duodenum, stomach and fundus. We are planning to use India ink dots to mark the esophagus every 1-2 cm to direct our biopsies and ensure the validity of the hyperspectral imaging. Dots will be placed submucosally via an endoscopic sclerotherapy needle. Images are obtained in the esophagus every 1-2 cm for the length of a Barrett's Segment. The esophagus is then washed with 10-20 cc of 1% acetic acid to disrupt the mucous layer on the surface of the esophagus. Imaging of the esophagus is repeated with biopsies being taken between "two" dots of India ink every 1-2 cm for the length of the Barrett's Segment. In addition to the above, two additional patient groups have been added to this study to include 5 with gastric cancer and 5 with esophageal cancer.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Enrolled subjects since last APR – 4

Adverse events – 0

Withdrawn patients – 0

New Literature – No new literature is available as to the efficacy of hyperspectral imaging in the gastrointestinal tract.

Four male patients aged 60 to 84 with LSBE (mean length 7 cm) were studied. The spectral signatures of normal and Barrett's esophagus were separated by more than ten degrees of vector angle derived from intensity differences. The mean spectral signature of fundic, Barrett's, and normal esophageal mucosa were each separated by six degrees. This level of separation allows for identification of specific mucosal features.

### CONCLUSIONS

None.



## DETAIL SUMMARY SHEET

**TITLE:** Twenty-Four Hour pH Monitoring and Histologic Evaluation in Patients With Tongues in the Distal Esophagus – Are These Findings Clinically Relevant?

**PRINCIPAL INVESTIGATOR:** Duncan, Marten, CPT MC

**ASSOCIATES:** Dr. Roy Wong, Corrinne Maydonovitch, and Eugenia Rueda-Pedraza

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Gastroenterology

**INITIAL APPROVAL DATE:** 17 September 2002

### STUDY OBJECTIVE

It is not known if a patient's distal mucosal tongue (a portion of stomach lining that protrudes into the esophagus) is related to gastroesophageal reflux disease. It is also not known to what extent distal mucosal tongues may be susceptible to the development of specialized intestinal metaplasia and malignancy as seen in patients with Barrett's esophagus. The goal of this study is to compare the degree of reflux in patients with distal mucosal tongues, patients with Short Segment Barrett's esophagus and patients with normal EGDs (esophagogastric duodenoscopy, also known as an upper endoscopy) by using 24-hour pH and manometric data.

### TECHNICAL APPROACH

This is a cross sectional study comparing four groups of patients attempting to determine the physiologic and histologic significance of distal esophageal mucosal tongues. The four study groups will be: A) Control group (normal EGD), B) 1cm distal mucosal tongues, C) 2cm distal mucosal tongues and D) SSBE (circumferential esophageal lesions under 3cm in length).

Enrolled patients will complete a confidential questionnaire pertaining to symptoms, personal habits and current medications. Patients will then undergo upper endoscopy with a standard diagnostic video endoscope and standard cold biopsy forceps. Tongues and other mucosal abnormalities will be measured during the upper endoscopy. The distal esophagus will be sprayed with 10 to 15 cc of 1.5% acetic acid using a spray catheter (Olympus, PW-5L-1) prior to biopsies to ensure that potential areas of SIM and dysplasia are not missed. This process disrupts the mucous layer present in the esophagus and produces reversible intracellular cytoplasmic denaturation enhancing the ability to detect small islands of columnar epithelium (14) and, thereby, improving biopsy accuracy. The lesions will be biopsied throughout their length for a goal of 4 to 8 biopsies per lesion. Four quadrant biopsies will be taken for every 2 cm of length for circumferential lesions.

Specimens, as per clinic SOP, will be sent to the Department of Pathology for preparation, sectioning and staining with hematoxylin and eosin to evaluate for evidence of either SIM or dysplasia. To provide consistency, histologic samples will be reviewed by Dr. Eugina Rueda-Pedraza. In addition, endoscopic measurements will be obtained including the length of a diaphragmatic hernia (if present), and the distance of the esophagogastric junction and the squamocolumnar junction from the incisors.

Subjects in groups B, C, and D will undergo esophageal manometry following the EGD – this will occur about 1 or 2 weeks after the endoscopy. The manometry study and pH study are performed at the same visit. Prolonged ambulatory pH monitoring will be performed with a portable pH monitor after completing the esophageal manometry. Prior to the pH study patients will be asked to discontinue all acid suppressing medications (including H2 blockers and proton pump inhibitors) for one week before the test. This is part of the standard preparation for pH testing to ensure medication effects are minimized. A monocrystalline antimony 4-channel pH electrode will be used with pH measurement sites at 0 cm, 1 cm, 2 cm, and 5 cm above the lower esophageal sphincter. This is a well established and standardized technique that is used at Gastroenterology clinics and referral centers. A silver chloride ECG reference electrode will also be used. All electrodes will be calibrated in

buffer solutions of pH 1,4, and 7. The electrode will be inserted through a nostril into the esophagus and position it at the lower esophageal sphincter (LES). The distance of the LES from the incisors will be predetermined during manometry. The electrode will be inserted in the clinic after which the subject will be sent home with an ambulatory halter monitor from Synetics, Inc. that will record the pH for 24 hours. Event buttons will allow subjects to record symptoms and activities that are correlated with esophageal pH. Reflux events will be defined as a drop in pH to below 4.0. This will provide important data for comparison of the degree of reflux between each study group. Specific parameters include esophageal amplitude, the 24-hour pH score, the percent time with reflux, the percent time with upright reflux, the percent time with supine reflux, and the lower esophageal sphincter pressure. Subjects will return to the clinic on the following day for removal of the electrode at which time, their participation in the study will be completed.

Patients in the control group (group A) will be consented for the study and asked to fill out a questionnaire in a clinic visit. After consent is obtained they will undergo the manometry and 24-hour pH study about 1-2 weeks after enrollment in the study. After this study their involvement will be complete.

There has been no deviation from the original protocol.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study enrollment and recruitment are ongoing. At this time, no new literature pertaining to the etiology of distal esophageal mucosal tongues and their physiologic and histologic makeup and is unchanged from when the study was originally submitted.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

#### CONCLUSIONS

No findings are available.

## DETAIL SUMMARY SHEET

TITLE: CALGB 79803 - Phase III Chemo Prevention Trial of Selenium Supplementation in Persons with Resected Stage I Non-Small Cell Lung Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J. COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 23 October 2001

### STUDY OBJECTIVE

To evaluate the efficacy of selenium supplementation in reducing the incidence of second-primary lung tumors in patients who have been treated for Stage I non-small cell lung cancer with complete surgical resection. To evaluate the qualitative and quantitative toxicity of a selenium supplementation in a daily administrative schedule. To compare the incidence of specific cancers and mortality from cancer as well as overall survival of patients treated with selenium supplementation versus patients treated with placebo.

### TECHNICAL APPROACH

This is a randomized phase III double-blinded, placebo-controlled study which means that participants would be randomized to receive either the selenium yeast tablets or placebo and neither patients nor investigators will know if they are on drug or placebo. There is an initial run-in period after registration to ensure compliance with the study drug prior to randomization. Patients are stratified according to smoking status and gender.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This is the first APR done on this study here at WRAMC. To date there have been no publications reporting data on this study or any study with similar design in literature.

The number of subjects enrolled to the study since last APR at WRAMC is N/A and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 188, if multi-site study. No grade 4 toxicities reported.

Ref: Jun 02 CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 19808 - Phase III Randomized Study of Induction Chemotherapy With or Without MDR-Modulation with PSC-833 (NSC #648265, IND #41121) Followed by Cytogenetic Risk-Adapted Intensification Therapy Followed by Immunotherapy with rIL-2 (NSC #373364, IND 1969) vs. Observation

PRINCIPAL INVESTIGATOR: Perkins, Jeremy G. CPT MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 29 November 2001

### STUDY OBJECTIVE

To determine whether the addition of PSC-833 to induction chemotherapy improves disease-free survival and overall survival for patients with AML <60 years. To determine whether post-consolidation immunotherapy with low-dose continuous/intermittent high-dose bolus subcutaneous rIL-2 improves disease-free survival and overall survival for patients with AML <60 years in first CR.

### TECHNICAL APPROACH

There are three parts to the treatment in this study: 1) Remission Induction Chemotherapy, 2) Intensification chemotherapy, and, if the patients is assigned to receive it, 3) Post-Remission Immunotherapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting any data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is N/A and the total enrolled to date at WRAMC is not approved yet. The total number enrolled study-wide is 114, if multi-site study. This study has not officially opened here at WR. Grade 4 toxicities include 51 neutrophils/granulocytes, 3 leukocytes, 6 hemoglobin, 45 platelets, 1 transfusion: platelets, 1 supraventricular arrhythmias, 1 hypotension, 1 cardiac-ischemia, 1 acute vascular leak syndrome, 1 DIC, 3 fatigue (lethargy/malaise), 2 anorexia, 4 dysphagia/esophagitis, 4 stomatitis, 1 CNS hemorrhage/bleeding, 1 hemorrhage/bleeding, 1 SGOT(AST), 1 SGPT(ALT), 1 bilirubin, 1 febrile neutropenia, 3 infection (documented clinical), 3 hypocalcemia, 2 hypokalemia, 1 hyperuricemia, 1 abdominal pain or cramping, 3 dyspnea (shortness of breath), 3 pneumonitis, 1 ARDS, 1 hypoxia, 1 pulmonary-other, and 1 renal failure. Grade 5 toxicities include 1 infection (documented clinical).

Ref: Jun 02 CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 99904 - Adjuvant Androgen Deprivation Versus Mitoxantrone Plus Prednisone Plus Androgen Deprivation in Selected High Risk Prostate Cancer Patients Following Radical Prostatectomy, Phase III

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J. COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 29 January 2002

### STUDY OBJECTIVE

The primary objective is to evaluate overall survival using adjuvant systemic therapy in high risk localized prostate cancer patients following radical prostatectomy. Disease-free survival will also be evaluated.

Patients will be randomized to one of the following arms:

- a. bicalutamide (Casodex®) + goserelin acetate (Zoladex®)
- b. mitoxantrone + prednisone administered with Casodex® + Zoladex®.

To compare qualitative and quantitative toxicity between the two study arms.

### TECHNICAL APPROACH

Basically patients will randomized to receive standard hormone therapy or standard hormone therapy with chemotherapy. Hormone therapy will last for two years. For those patients randomized to hormonal and chemotherapy, the chemotherapy will be given simultaneously with the hormonal for six cycles of 21 days. A comprehensive calendar will be developed for each patient.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this study since its activation.

The number of subjects enrolled to the study since last APR at WRAMC is N/A and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 175, if multi-site study. No adverse events reported. No toxicities reported.

Ref: Nov 02 CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 79806 Effects of Dietary Soy on Biomarkers of Prostate Cancer – A Prospective Phase II Study

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J. COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: O  
INITIAL APPROVAL DATE: 14 May 2002

### STUDY OBJECTIVE

To test the hypothesis that 25 grams of soy protein (with 52mg isoflavones) as a daily supplement for a period of twelve months will reduce prostatic cellular proliferation rates by 50% (as measured by Ki-67) in men aged 50 and over with an elevated PSA of 5-10 ng/ml but a biopsy negative for prostate cancer as compared to 25 grams of casein protein (without isoflavones).

To measure the effects of soy supplementation on additional biomarkers of prostate cancer (serum PSA, high-grade prostate intraepithelial neoplasia (PIN), induction of apoptosis, sex steroid receptor expression, and loss of GST-pi).

To measure the effects of soy supplementation of health-related quality of life (including urinary and sexual function).

### TECHNICAL APPROACH

After patients are determined eligible, they will be asked to return for the run-in visit. At this visit participants will undergo a digital rectal exam, have blood drawn, and be asked to complete the participant questionnaires. Participants will then enter a two-week run-in period during which they will be asked to take the casein supplement daily. If the participant consumes at least twelve of the packets during this period, he will be considered compliant and eligible for randomization. Participants are then randomized to take either 25 grams of soy protein containing 52mg of isoflavones or 25 grams of casein protein (placebo) containing 0 mg of isoflavones daily for twelve months.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is N/A and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 6, if multi-site study. No grade 4 toxicities reported. This study was temporarily suspended effective January 6, 2003.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 40101/CTSU 40101 – Cyclophosphamide and Doxorubicin (CA) (4 Versus 6 Cycles) Versus Paclitaxel (12 Weeks Versus 18 Weeks) as Adjuvant Therapy for Women With Node Negative Breast Cancer – A 2x2 Factorial Phase III Randomized Study

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J. COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 13 August 2002

### STUDY OBJECTIVE

To determine the equivalence of weekly Paclitaxel with CA as adjuvant therapy for women with high-risk node-negative breast cancer for disease-free survival.

To determine if longer therapy, 18 weeks, is superior to shorter therapy, 12 weeks, of either CA or Paclitaxel for disease-free survival for women with node-negative breast cancer.

### TECHNICAL APPROACH

The patients on this study have node-negative breast cancer. The patient has had surgical removal of the breast cancer and the doctor has determined that adjuvant chemotherapy is advisable for the stage of breast cancer the patient is in.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 7. The total number enrolled study-wide is 17, if multi-site study. No Grade 4 toxicities reported. Adverse event reported April 3, 2003.

Ref: CALGB Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: CALGB 30102 – Phase III Comparison of Catheter Based Therapy of Pleural Effusions in Cancer Patients (Optimal Pleural Effusion Control, OPEC)

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 27 August 2002

### STUDY OBJECTIVE

To compare the proportion of patients with symptomatic malignant pleural effusions who are successfully treated and maintain effusion control at 30 days after treatment. The treatment for a malignant pleural effusion will be considered “successful” if:

- Patient does not die within 30 days of the procedure.
- Effusion does not recur within 30 days of the initial procedure.
- The randomized effusion control procedure has been completed and has achieved reliable and consistent function within a clinically tolerable interval of 2 weeks.
- Lung re-expansion  $\geq 90\%$  after desired effusion is drained.
- Chest tube removed within 14 days of placement.

### TECHNICAL APPROACH

These patients have fluid in their chest, which is caused by malignant pleural effusion. Doctors use a variety of methods to treat pleural effusions, such as draining the fluid with a needle or a tiny tube, medications, or other methods. However, it is not known which method works best.

There will be treatment    Group A: Placement of a chest tube with talc therapy  
                                      Group B: Placement of a small (Pleur X) tube without  
                                      medications or chemicals.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting any data on this study.

The number of subjects enrolled to the study since last APR at WRAMC is N/A and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 18, if multi-site study. No grade 4 toxicities reported.

### CONCLUSIONS

Too early.



## DETAIL SUMMARY SHEET

TITLE: An Open-Label, Randomized Study to Develop a Screening Tool for Functional Capacity in Anemic Subjects with Nonmyeloid Malignancies Receiving Chemotherapy and Darbepoetin Alfa (NESP)

KEYWORDS: Screening Tool, Anemic patients, Chemotherapy, Darbepoetin Alfa (NESP)

PRINCIPAL INVESTIGATOR: Myhand, Ricky LTC MC

ASSOCIATES: COL Joseph Drabick MC, MAJ Carl Willis MC, MAJ Jamie Waselenko MC

DEPARTMENT: Medicine

STATUS: C

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 23 April 2002

### STUDY OBJECTIVE

To develop a functional capacity screening tool (FCST) that estimates at baseline the functional capacity of anemic subjects with nonmyeloid malignancies receiving multiple chemotherapy.

To assess the relationship between hgb response and change in functional capacity.

### TECHNICAL APPROACH

Please refer to the sponsor's protocol.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 1570, if multi-site study.

### CONCLUSIONS

No patients were enrolled at WRAMC. Amgen closed the study in December of 2002. Therefore, no patients will be enrolled from WRAMC. We would like this study officially closed.

## DETAIL SUMMARY SHEET

**TITLE:** Randomized Study of Fludarabine and Cyclophosphamide With or Without Genasense (Bcl-2 Antisense Oligonucleotide) in Patients With Relapsed Chronic Lymphocytic Leukemia (Protocol GL303)

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** Waselenko, Jamie K. MAJ MC  
**ASSOCIATES:**

**DEPARTMENT:** Medicine  
**SERVICE:** Hematology-Oncology

**STATUS:** C  
**INITIAL APPROVAL DATE:** 11 June 2002

### STUDY OBJECTIVE

The primary objective is to compare the proportion of patients with relapsed or refractory CLL randomized to treatment with fludarabine plus cyclophosphamide (Flu/Cy) versus patients randomized to treatment with Flu/Cy combined with Genasense who achieve complete response (CR) or nodular partial response (n-PR).

The secondary objective is to compare proportional differences between the two treatment groups in overall response rate (CR + n-PR + PR), survival, duration of response, time to progression, clinical benefit, and safety. (Measures of clinical benefit include: resolution of B-symptoms (fever, night sweats, early satiety due to hepatosplenomegaly, abdominal discomfort due to hepatosplenomegaly, impaired cosmesis due to lymphadenopathy, impaired mobility due to lymphadenopathy), resolution or reduction in massive splenomegaly, change in performance status, and improvement in disease-related anemia.

### TECHNICAL APPROACH

This is a Phase III, open-label, multicenter, randomized study. Patients will be randomized in a 1:1 ratio to Flu/Cy + Genasense or Flu/Cy alone.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is unknown, if multi-site study.

Several safety reports regarding potential adverse events related to the study drug have been published and are filed with DCI.

An addendum is being reviewed by DCI for the addition of new risks to the consent form.

### CONCLUSIONS

No conclusions can be reached at this time.  
Study closed to enrollment as of 15 June 2003.

## DETAIL SUMMARY SHEET

TITLE: Collection of Blood Components From Healthy Donors For In Vitro Research – WRAIR Protocol # 837

PRINCIPAL INVESTIGATOR: Babcock, Janine COL MC

ASSOCIATES: MAJ Francis Chiricosta MC, LTC Frank Rentas MS, MAJ Lloyd Ketchum, MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 11 June 2002

### STUDY OBJECTIVE

The WRAIR HUC judged this protocol to present no greater than minimal risk in November 2001 and permission was granted to begin enrolling volunteers only for participation at WRAIR (no apheresis). This CR report does contain information dating to December 2001 for the volunteers enrolled for participation at WRAIR. The WRAMC IRB ruled that apheresis does present greater than minimal risk, and the protocol then required review at the HSRRB level. No volunteer was enrolled for a project involving apheresis, which is performed at WRAMC, until after 20 September 2002, the date of HSRRB approval. This protocol was granted a waiver from the Volunteer Database Registration requirement by the HSRRB.

As WRAIR is the IRB of record, the protocol follows WRAIR's privacy/HIPAA policy. This protocol is designed to provide a mechanism to collect and process blood components from consented, healthy, volunteer donors for distribution to WRAIR scientists for *in vitro* research. The intent of this protocol is not to approve the research itself, but to provide adequate and complete informed consent for the donor and to assure that the education, counseling, and protection of the research blood donors is performed in accordance with IRB, DA, OHRP, and other applicable federal regulatory standards.

### TECHNICAL APPROACH

Volunteers meeting standard blood donor eligibility criteria are recruited to donate blood and blood components by standard phlebotomy and apheresis techniques. The investigational nature of the studies in which their blood will be used and the risks and discomforts of the donation process are explained to the donors. An informed consent document is reviewed with the volunteers. They have several opportunities to ask questions, and they are asked to sign if they would like to participate. Volunteers choose which type of donation procedures they are willing to undergo. They undergo a brief screening examination, and baseline blood tests are drawn to confirm normal blood counts and exclude donors with transfusion-transmitted diseases. Based on the screening results, donors are enrolled into the study to perform specific donation procedures based on their preferences and lab results. The protocol provides a schema for safety monitoring of repeat donors to prevent complications of excessive phlebotomy. It also provides the mechanism to ensure donor confidentiality and proper disposal of the blood products.

WRAIR scientists requesting blood components for research submit a written memo to the Department of Clinical Trials (DCT) describing their project. The memo includes a brief summary of the research, and provides assurance that samples provided for the project will be used solely for *in vitro* research. Each project is reviewed by the PI for appropriateness, feasibility, and compliance with ethical and regulatory standards. The project is submitted to the WRAIR Office of Research Management for scientific review by a scientist external to the protocol and then submitted for expedited review by the WRAIR HURC.

**PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE**

Literature review found five articles relevant to study. Since the study opened in December 2001, the number of volunteers enrolled is 54. (This is the first continuing review report.) We define a volunteer as enrolled for the study when they have complied with a scheduled visit and attempted one donation. 109 volunteers were scheduled to come in to the Clinical Trials Center to brief. 84 have actually attended briefings. All 84 who were briefed gave consent. 61 qualified to participate, but seven have not yet made a donation.

There have been three protocol deviations, all submitted since 15 March 2003. All of the deviations have involved fairly minor errors with the apheresis technician. They have been addressed by counseling sessions, review of protocol requirements, review of GCP/ICH practices, and plans for formal GCP training.

**CONCLUSIONS**

This service protocol is actively supporting research in four WRAIR departments with a good safety record. There have been no SAEs and no adverse events documented. Two deviations have occurred, but there is not a pattern of repeated mistakes suggesting that counseling and training are achieving their objectives. A revised protocol is submitted including minor revisions that are detailed in a separate memo.

## DETAIL SUMMARY SHEET

TITLE: A Phase II Study of the Recombinant Human Monoclonal Anti-Bascular Endothelia Growth Factor Antibody (rhuMAB VEGF) Bevacizumab Administered in Timed Sequential Combination with Cytosine Arabinoside (ara-C) and Mitoxantrone for Adults with Refractory and Relapsed Acute Myelogenous Leukemias (AMLs)

KEYWORDS:

PRINCIPAL INVESTIGATOR: Waselenko, Jamie K. MAJ MC

ASSOCIATES:

DEPARTMENT: Medicine

SERVICE: Hematology-Oncology

STATUS: W

INITIAL APPROVAL DATE: 16 July 2002

### STUDY OBJECTIVE

Study withdrawn.

### TECHNICAL APPROACH

Study withdrawn.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn.

### CONCLUSIONS

Study withdrawn.

## DETAIL SUMMARY SHEET

**TITLE:** Phase II Randomized Trial of High Dose Busulfan and Thiotepa With Autologous Peripheral Blood Stem Cell (PBSC) Support Versus Standard Dose Docetaxel and Estramustine Regimen For Treatment Of Hormone Refractory Metastatic Prostate Cancer

**KEYWORDS:** Busulfan, Thiotepa, Autologous Peripheral Blood Stem Cell, PBSC Support, Docetaxel, Estramustine, refractory metastatic prostate cancer

**PRINCIPAL INVESTIGATOR:** Myhand, Rickey C., LTC MC

**ASSOCIATES:** COL Joseph Drabick, MC, MAJ Carl Willis, MC, MAJ Jamie Waselenko, MC

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Hematology-Oncology

**INITIAL APPROVAL DATE:** 6 August 2002

### STUDY OBJECTIVE

To compare the progression-free survival rate at one year for treatment of hormone-refractory metastatic prostate cancer among patients randomized to high dose therapy followed by autologous PBSC rescue or conventional therapy.

### TECHNICAL APPROACH

Patients will be informed of the investigational treatment versus conventional treatment on this study. A consent form will be given to the patient for their review and time will be given to the patient to answer their questions. Their oncologist will explain this study to them and an oncology research nurse before the patient consents to participation. Pre-study exams, which are routine, will be performed to assure eligibility and to provide baseline tumor measurements, which will be used for response to treatment. All patients will undergo apheresis. Randomization to high dose chemotherapy (HDC) with peripheral blood stem cell transplant or to conventional therapy will be computer generated. This study has a crossover design if patient progresses or does not respond after initial treatment. All patients will have a central catheter placed before any treatment is started. High dose chemotherapy patients will most likely require hospitalization because of the intensity of the doses given. Re-staging on the HDC arm will be done two months after HDC and then every three months for one year, then every six months for four years, then yearly. Re-staging on the conventional arm will be done every three cycles. After conventional therapy ends due to a complete response, progressive disease, or intolerable side effects, re-staging will be done every three months for one year, then every six months for four years, then yearly. There is a quality-of-life questionnaire that will be done four times during the first year.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This protocol is being done in collaboration with the Fred Hutchison Cancer Research Center. There has been only one patient accrued to this study by the Fred Hutchison Cancer Research Center. No serious adverse events have been reported. No patients have been enrolled at WRAMC. Only one patient has been referred for counseling at WRAMC, and his eligibility is still being determined. Determination to continue this study, given the poor accrual, will be made in October of 2003 when the study is due for local (FH) annual review.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 1, if multi-site study.

### CONCLUSIONS

No conclusions have been made. This study may be closed in October of 2003 due to lack of accrual.

## DETAIL SUMMARY SHEET

TITLE: A Phase II Clinical Trial of BMS-247550 (NSC #710428) – An Epothilone B Analog in Patients With Breast Carcinoma

KEYWORDS: breast cancer, epothilone, metastatic, taxanes

PRINCIPAL INVESTIGATOR: Waselenko, Jamie D., MAJ MC

ASSOCIATES: Drabick, Joseph, COL MC, Willis, Carl, MAJ MC, Myhand, Rick, LC MC, Statler, John, MAJ MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 13 August 2002

### STUDY OBJECTIVE

1. To establish the anti-tumor activity of the epothilone B analog, BMS-247550 administered daily in patients with metastatic breast carcinoma. Patients will be stratified by prior taxane therapy versus taxane-naïve.
2. Assess the toxicity of BMS-247550 with this treatment regimen.
3. Evaluate mechanisms of drug resistance by examining the tumor polymerization by immunohistochemistry from obtained biopsy specimens.

### TECHNICAL APPROACH

Patients will receive BMS-247550 daily as a one-hour infusion on five successive days (daily x 5 at 6mg/m<sup>2</sup>/day) every 21 days in patients with metastatic breast carcinoma. They will be treated in the outpatient clinic.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This protocol is being conducted as an affiliate site for the National Cancer Institute at the National Institutes of Health. The study has been approved for 58 patients (37 who have received prior taxane treatment and 21 patients who are taxane naïve). Twenty safety reports received from the NCI have been filed with the IRB. None involved patients treated on this protocol. They were patients receiving the investigational drug BMS-247550 on other studies and with a variety of diagnoses. Of the 28 patients that have been enrolled on this study (zero here at WRAMC), four are still too early to evaluate. Of the 18 who have received prior taxane therapy, there were five patients with partial responses (one unconfirmed), six with stable disease, and seven progressive disease. Of the six patients who have been taxane-naïve, there were four partial responses (one unconfirmed), and two with stable disease.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 28, if multi-site study.

### CONCLUSIONS

This study is still ongoing and no conclusions can be reached yet.

## DETAIL SUMMARY SHEET

TITLE: Tc-99m Depreotide Scanning in Sarcoidosis

KEYWORDS: Sarcoidosis, Nuclear imaging

PRINCIPAL INVESTIGATOR: Shorr, Andrew F. MAJ MC

ASSOCIATES: Robert Bridwell, Donald Helman

DEPARTMENT: Medicine

STATUS: O

SERVICE: Pulmonary & Critical Care Medicine

INITIAL APPROVAL DATE: 23 October 2001

### STUDY OBJECTIVE

To determine the incidence of positive Tc-99m Depreotide scans in patients with sarcoidosis and to correlate the results of these scans with standard markers of disease activity.

### TECHNICAL APPROACH

Patients who consent to be in the study have this imaging done in nuclear medicine. Results are correlated with clinical findings done as part of the routine evaluation for the follow-up of patients with sarcoidosis. (Simple, cross-sectional design of a convenience sample.)

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No studies thus far have been published in this area, as this technology is very novel and WRAMC is a center of excellence in its developments. (We have a number of ongoing studies using this test in a number of conditions.) We have enrolled 13 of a planned 100 patients, so it is too soon to examine the data. The number of subjects enrolled to the study since last APR at WRAMC is 13, and the total enrolled to date at WRAMC is 13. The total number enrolled study-wide is 13, if multi-site study.

### CONCLUSIONS

None so far.



## DETAIL SUMMARY SHEET

TITLE: Patterns of Oropharyngeal Bacterial Colonization after Hospitalization

KEYWORDS: Colonization, Pneumonia, Nosocomial, Risk Factor

PRINCIPAL INVESTIGATOR: CPT Donald Helman MC

ASSOCIATES: CPT Kevin Woods, LTC Lisa Moores, LTC Glenn Wortmann, LTC David Craft, LTC Joel Fishbain, Mrs. Robin Howard

DEPARTMENT: Medicine

STATUS: O

SERVICE: Pulmonary & Critical Care Medicine

INITIAL APPROVAL DATE: 23 April 2002

### STUDY OBJECTIVES

Primary objective: Determine the rates of abnormal oropharyngeal bacterial colonization (presence of enteric gram negative bacilli) in subjects at the time of hospital discharge and at 2, 4, and 8 weeks post-discharge. Compare these colonization rates to non-hospitalized matched controls.

Secondary objectives: Explore factors that influence colonization after discharge. (Specifically evaluating: age, history of diabetes, history of chronic obstructive pulmonary disease (COPD), length of hospitalization, requirement for intensive care unit (ICU) care, duration of ICU care, endotracheal intubation, nasogastric intubation, duration of mechanical ventilation, admission APACHE II score, use of medications altering gastric pH, use of corticosteroids, current & former tobacco use, and the use of broad spectrum antibiotics).

### TECHNICAL APPROACH

Hospitalized patients will be approached and, if informed consent is obtained, will have a sterile saline gargle performed on the day of discharge. Only patients hospitalized  $\geq 72$  hours will be eligible to participate in the study. Internal medicine house-staff will be the primary individuals identifying patients who would be eligible for study enrollment. At the time of discharge, these house-staff will determine if patients meet inclusion/exclusion criteria then they will be given an opportunity to review the consent form and ask questions of the associate investigators. Data will be collected from their inpatient medical record and entered onto Appendix 1 – Hospitalized Data Collection Sheet. All subjects will be asked to return to the WRAMC Infectious Disease or Pulmonary clinic at 2, 4 and 8-weeks following discharge date for a sterile gargle. All subjects, regardless of colonization status at the time of discharge, will be asked to return at the 2, 4, and 8-week time points.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

In the interval since protocol approval, only one study that I am aware of has been published that significantly affects our project (Arancibia et al. Community-acquired pneumonia due to gram-negative bacteria and *Pseudomonas aeruginosa*, Arch Intern Med 2002;162:1849-1858). These investigators prospectively evaluated patients admitted with community-acquired pneumonia (CAP) and determined risk factors for CAP due to gram-negative bacteria. Among their findings, they noted that the most significant risk factor for CAP with these organisms was previous hospital admission within the previous 30 days (OR 3.5). Our project has not enrolled sufficient numbers as to make even preliminary findings. There have been no adverse events associated with this protocol. The number of subjects enrolled to the study since last APR at WRAMC is 13 and the total enrolled to date at WRAMC is 13.

### CONCLUSIONS

No conclusions can be made at this time.

## DETAIL SUMMARY SHEET

**TITLE:** Comparison of Efficacy and Safety of Zolpidem-MR 12.5 mg and Placebo in Patients With Primary Insomnia – A Double-Blind, Randomized, Placebo-Controlled, Parallel-Group Study

**KEYWORDS:** insomnia, Zolpidem, Ambien

**PRINCIPAL INVESTIGATOR:** Kristo, David LTC MC

**ASSOCIATES:** Teotimo Andrada MS RPSGT, COL Arn H. Eliasson MC, LTC Paula Ephraim AN (Ret.) MSN RN, Andrei Khramtsov MD, Yvonne Taylor RN DRPh (c)

**DEPARTMENT:** Medicine

**STATUS:** C

**SERVICE:** Pulmonary & Critical Care Medicine

**INITIAL APPROVAL DATE:** 23 April 2002

### STUDY OBJECTIVE

- To evaluate the hypnotic efficacy of Zolpidem-MR 12.5 mg compared to placebo using polysomnogram and patient sleep questionnaires.
- To evaluate the residual effects that may be associated with Zolpidem-MR 12.5 mg as compared to placebo following each of the 21 nights of treatment.
- To compare the effect on sleep following abrupt discontinuation between Zolpidem-MR 12.5 mg and placebo after 21 nights of treatment.
- To evaluate the clinical safety and tolerability of Zolpidem-MR 12.5 mg compared to placebo.

### TECHNICAL APPROACH

This thirty-day study for adults with primary insomnia involved a screening phase, a treatment phase, and a run-out phase. Screening included a visit in the Sleep Clinic, followed by two consecutive nights of polysomnographic screening in the sleep lab. Treatment consisted of two consecutive nights of PSG in the sleep lab with double-blind treatment for insomnia, followed by twelve nights of outpatient double-blind study treatment, followed by two consecutive nights of PSG in the sleep lab with double-blind study treatment for insomnia, followed by five nights of outpatient double-blind study treatment. The run-out phase required two consecutive nights of PSG in the sleep lab with single-blind placebo. No modifications to the protocol were made following DCI approval.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

DCI approval to begin work on this protocol was issued 29 August 2002 after we had received notice from the sponsor on 27 August 2002 that they were suspending enrollment in the US as a result of reaching their enrollment quota earlier than expected. A formal letter from the sponsor stating that enrollment goals had been achieved and that our participation in the study was no longer possible was received in late September. As we did not enroll anyone, we also did not receive notice of any adverse events that may have occurred at other locations. As WRAMC is a non-participant, there is no continuing review of literature or any research findings to report.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 200, if multi-site study.

### CONCLUSIONS

The protracted approval process at WRAMC delayed our participation in this challenging study to the point that we were non-competitive with the civilian sector. This study is closed without any findings or conclusions.

## DETAIL SUMMARY SHEET

TITLE: Vocal Cord Dysfunction and Hyperventilation – Do They Coexist?

KEYWORDS:

PRINCIPAL INVESTIGATOR: Parker, Joseph M. LTC MC

ASSOCIATES: MAJ David Brown

DEPARTMENT: Medicine

STATUS: O

SERVICE: Pulmonary & Critical Care Medicine

INITIAL APPROVAL DATE: 28 May 2002

### STUDY OBJECTIVE:

Determine the relationship between vocal cord dysfunction and hyperventilation with exercise.

### TECHNICAL APPROACH:

No modifications to original protocol have been made.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The Principal Investigator at USUHS transferred to another location and an alternate investigator has not been identified. Until a new investigator at USUHS is identified no work will be forthcoming on this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

### CONCLUSIONS:

None.

## DETAIL SUMMARY SHEET

TITLE: Perioperative Beta-Blockade in Patients With Chronic Obstructive Pulmonary Disease

PRINCIPAL INVESTIGATOR: Johnson, Scott J., MAJ MC

DEPARTMENT: Medicine

STATUS: O

SERVICE: Pulmonary &amp; Critical Care Medicine

INITIAL APPROVAL DATE: 16 July 2002

STUDY OBJECTIVE:

To demonstrate the safety of oral Atenolol given perioperatively to patients with COPD, a group in which beta-blockers has traditionally been considered relatively contraindicated.

TECHNICAL APPROACH:

This study is designed as a prospective, randomized, double blind, placebo-controlled clinical trial. Patients will be randomized into peri-operative treatment with either Atenolol or placebo. Oral preparations of the active drug and placebo will be prepared by the Clinical Research Pharmacy and administered according to a computer-generated, randomized list that will be retained only by the pharmacy. All patients will be treated with peri-operative bronchodilators (Atrovent +/- Albuterol), which are considered to be standard of care for patients with COPD undergoing any surgical procedure. Primary outcome measures will be phenomena that might be attributed to adverse complications of beta-blocker drugs: bronchospasm; any respiratory infection, complication, or complaint, including wheezing, coughing, dyspnea; bradycardia; heart block; pulmonary congestion. NOTE: It is recognized that many of these complications including pulmonary congestion and/or hypotension may occur unrelated to beta-blocker toxicity. Discontinuation of the study drug will only occur upon decisions made by investigators and/or attending physicians. Patients enrolled in the study will be given the study agent (Atenolol vs. placebo) dispensed from the Clinical Research Pharmacy with instructions to take 1 capsule (50mg) a day beginning 5 days prior to surgery. If surgery is scheduled for less than 5 days hence, the patient will still be enrolled and the study medication will be started immediately. For those patients taking the study medication 3 days or less before surgery, no medication dose adjustment will be made. For patients taking the medication 4-5 days before surgery, the enrolling investigator will call the patient on day 3 to obtain current heart rate information and any possible side effects. The study medication dose will then be adjusted according to heart rate (hold if HR < 55; one capsule (50mg) for HR 55-64; two capsules (100mg) for HR ≥ 65). On the day of surgery, spirometry will be performed preoperatively prior to administering the daily dose of study drug (atenolol or placebo). Patients will bring their study medication for the day of surgery only. All other study medications to be dispensed from the Clinical Research Pharmacy while in the hospital. A reduction in FEV1 from baseline level of 15% will prompt a call to one of the investigators who will then inform the anesthesiologist and surgeon that surgery ought to be delayed until the study drug is stopped, appropriate bronchodilator medication is given, and FEV1 returns towards baseline. Significant symptomatic wheezing or evidence of airflow obstruction may cause surgery to be canceled. We consider this eventuality to be unlikely (less than 5%).

For the majority of patients whose FEV1 has not decreased > 15% from baseline, study drug will be continued on the day of surgery and each day post-op *while hospitalized* up to 14 days. Patients discharged home prior to day 7 will continue their medication for a total of 7 days post-op and have follow up by telephone by either the principal investigator or one of the associate investigators using an approved script. If discharged on days 8-14 post-op, no further study medication will be given. While hospitalized, patients will be assessed daily and the information recorded by one of the investigators. Any adverse events will be documented on the patient's study data collection sheet. We hypothesize that the incidence of such events is likely to be low.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Enrollment at WRAMC has been extremely slow. Since final approval of the study, the Principle Investigator has been on clinical rotations at outside hospitals for 4 of the past 7 months, and, as a result, attempts at educating health care providers working in areas of potential recruitment have fallen short. As a new academic year is about to begin, the current PI will be transferring to a new duty station and a new Principle Investigator will take over. Dr. Jeffrey Mikita, one of the associate investigators, has been accepted into the pulmonary fellowship here at Walter Reed and has agreed to be the new PI. As a first year fellow, the majority of Dr Mikita's clinical responsibilities will be at WRAMC, and, as such, will be able to more closely monitor and facilitate the education and enrollment process. The main catchment area for potential patients is the Pulmonary Functions Lab, located in the Pulmonary Clinic. As a Pulmonary Fellow, Dr Mikita will be working very closely on a daily basis with the technicians in the PFT lab and can facilitate a more efficient enrollment process. Similar problems have been experienced at Portsmouth Naval Hospital, where the PI and some of the AIs were deployed with the Navy in support of the military operations in Iraq. As a result, enrollment of patients has not occurred over the past 8 months. Dr. Rascona (the study's over-all PI) has since returned and expects to be enrolling patients again soon.

The number of subjects enrolled to the study since last APR (enrollment began Oct 2002) at WRAMC is 1 and the total enrolled to date at WRAMC is 1. The total number enrolled study-wide is 17, if multi-site study. There have been no serious adverse events at Walter Reed or Portsmouth Naval Hospitals.

#### Review of recent literature:

Since the beginning of this study, there have been three reports published in the literature, all by the same authors, reviewing the same data<sup>1-3</sup>. These reports are a meta-analysis of all randomized, blinded, placebo-controlled trials from 1966 to May 2001 that studied the effects of cardioselective beta-blockers on FEV1, symptoms, and the use of inhaled beta2-agonists in patients with reactive airway disease. Nineteen studies on single-dose treatment and 10 studies on continued treatment were included. No significant treatment effect in terms of FEV1 was found in patients with concomitant chronic obstructive pulmonary disease. The authors concluded that cardioselective beta-blockers do not produce clinically significant adverse respiratory effects in patients with mild to moderate reactive airway disease or COPD, and that given the benefit of such medications, they should not be withheld from these patients. They also comment that these results were obtained in a small number of studies of few patients, and further studies with larger patient cohorts needs to be carried out. The specific population of patients being studied by our protocol does not appear to be represented in these reviews. These literature reviews have found articles regarding the use of beta-blockers for short-term or outpatient use, but not for short-term perioperative use. These reviews do suggest that the use of cardioselective beta-blockers is safe in patients with obstructive lung disease, which is the operative hypothesis of our protocol.

1. Salpeter SR, Ormiston TM, Salpeter EE. Cardioselective beta-blockers in patients with reactive airway disease: a meta-analysis. *Ann Intern Med* 2002 Nov 5;137(9):715-25
2. Salpeter SR, Ormiston TM, Salpeter EE. Cardioselective beta-blockers for reversible airway disease. *Cochrane Database Syst Rev* 2002;(4):CD002992
3. Salpeter SR, Ormiston TM, Salpeter EE, Poole P, Cates C. Cardioselective beta-blockers for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2002;(2):CD003566

#### CONCLUSIONS

Given the lack of clinical trials enrolling large numbers of patients with COPD in a perioperative period, our study is very important in providing useful information regarding the safety of cardioselective Beta-blockade medications in patients with COPD undergoing elective or semi-elective surgery. With the changes in PI, the enrollment process should be greatly enhanced.

## DETAIL SUMMARY SHEET

TITLE: Reference Values for Impulse Oscillometry in Normal Adults

KEYWORDS: Pulmonary Function Testing; Impulse Oscillometry

PRINCIPAL INVESTIGATOR: Hnatiuk, Oleh LTC MC

ASSOCIATES: Sierra, Angel

DEPARTMENT: Medicine

STATUS: O

SERVICE: Pulmonary & Critical Care Medicine

INITIAL APPROVAL DATE: 16 July 2002

### STUDY OBJECTIVE

To establish reference values for impulse oscillometry in a population of normal adults.

### TECHNICAL APPROACH

No modifications to the study have been made. The study design is a multi-center, prospective cohort trial to establish the first patient reference data set for impulse oscillometry in the United States for both non-white and Caucasian populations. Each subject will perform screening spirometry in accordance with ATS Guidelines.<sup>1</sup> If spirometry is normal, each subject will then undergo testing using the FDA approved, WRAMC owned, impulse oscillator (Jaeger Masterscreen IOS model 176450, Millibury, OH) with the Sensormedics Freeflow mouthpiece. The subject will perform three upright, seated oscillometry measurements, supporting their cheeks with their hands, and breath normally into a mouthpiece for 30 to 60 seconds while each oscillometry measurement is performed using standard technique.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been no new literature published in the last year affecting this study. The study has not begun accruing patients because the pilot study, with the same name, just completed data collection. We are analyzing that data to decide what mouthpiece to use in the current study. Also, the war in Iraq has significantly decreased the number of potential subjects at surrounding military installations, Fort Bragg, and Fort Bliss (through deployment). The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0.

### CONCLUSIONS

The study is slow getting started due to having to wait for pilot study completion and the war in Iraq. We anticipate the pace of subject accrual to hasten in the coming year.

## DETAIL SUMMARY SHEET

**TITLE:** Pulmonary Aspiration of Enteral Feeding in Critically Ill Patients – Incidence, Clinical Significance, and Usefulness of Bedside Diagnostic Testing

**KEYWORDS:** Aspiration, Enteral Feeding, Glucose Oxidase Testing, Mechanical Ventilation

**PRINCIPAL INVESTIGATOR:** Greenberg, Bruce A., CPT MC

**ASSOCIATES:** MAJ Stuart A. Roop, MAJ Brian Cuneo, MAJ Jaime L. Montilla, MAJ Robert Bridwell, MAJ Karen Whitman, Nagla Wahab, PhD

**DEPARTMENT:** Medicine

**STATUS:** O

**SERVICE:** Pulmonary & Critical Care Medicine

**INITIAL APPROVAL DATE:** 17 September 2002

### STUDY OBJECTIVE:

To determine the incidence of pulmonary aspiration during enteral tube feeding in ventilated intensive care unit patients as detected by bedside diagnostic techniques and clinical parameters.

To measure the relative sensitivity of glucose oxidase testing of tracheal aspirates compared to measuring radiotracer activity in bronchial secretions (using radiolabeled tube feeding) for detection of pulmonary aspiration.

To measure the specificity of glucose oxidase testing of tracheal secretions by testing secretions from a control group of mechanically ventilated patients not receiving tube feeding.

To explore the association, if any, between “sub-clinical” pulmonary aspiration of enteral feeding and the development of clinically apparent aspiration or nosocomial pneumonia.

### TECHNICAL APPROACH

This is a prospective study with two phases. Phase one will include ten patients who are intubated and receiving mechanical ventilation but are not being enterally fed. Samples of the tracheal aspirate obtained as part of routine care in the intensive care unit will be assayed to determine the level of background radiation in patients not being enterally fed. Phase two will enroll up to 70 patients who have been enterally fed for up to 72 hours. They will be fed in accordance with the WRAMC ICU enteral feeding protocol. Once per 24 hours for three days one bag of tube feeding will be radiolabeled with 1 mCi of Tc99m-SC. Tracheal aspirates will be assayed to determine level of radioactivity. Both phase one and two patients will be followed clinically for the development of infiltrates on chest X-ray, development of pneumonia, character and volume of tracheal secretions. All tracheal aspirates will be tested for glucose using bedside reagent strips. All patients will be followed for up to 30 days after enrollment to determine subsequent clinical course, especially the development of pneumonia.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have to my knowledge been no significant new studies published involving the glucose oxidase bedside test to determine aspiration. Since last review, surrogate consent has not been approved, and patients will only be enrolled if they are able to give witnessed, informed consent.

No patients have yet been enrolled. There have been no adverse events.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

We have recently received approval to start enrolling patients, and will begin once this annual progress report is reviewed.

## DETAIL SUMMARY SHEET

TITLE: In Vitro Immunogenicity Assessment of HIV Vaccine Candidates

KEYWORDS:

PRINCIPAL INVESTIGATOR: Mary A. Marovich (PI change ongoing)

ASSOCIATES: Josephine Cox

DEPARTMENT: Medicine

SERVICE: Infectious Disease

STATUS: O

INITIAL APPROVAL DATE: 9 April 2002

### STUDY OBJECTIVE:

Obtain peripheral blood mononuclear cells from HIV seropositives, as a source of sensitized T cells, for use in HIV vaccine development research.

### TECHNICAL APPROACH

Leukapheresis performed on healthy seropositive individuals for in vitro laboratory use only.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No enrollees. Study not started yet.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0 if multi-site study.

Please note this study is NOT open yet. While it may have been approved by DCI last April, it is still undergoing revisions for ultimate approval by MRM/HSRRB.

### CONCLUSIONS

None.



## DETAIL SUMMARY SHEET

TITLE: Validation of a Diagnostic Algorithm for the Evaluation of Nosocomial Febrile Illness

KEYWORDS: Nosocomial, Fever

PRINCIPAL INVESTIGATOR: Dr Timothy Straight (CPT, MC, USA)

ASSOCIATES: Dr Joshua Hartzell (CPT, MC, USA), Dr Ramey Wilson (CPT, MC, USA), Dr William Bimson (CPT, MC, USA), Dr Pram Verma (CPT, MC, USA), Dr Charles Oster (COL, MC, USA)

COLLABORATORS: Mrs. Donna Vieira B.S.N., R.N., Dr. Thomas Boal

DEPARTMENT: Medicine

STATUS: O

SERVICE: Infectious Disease

INITIAL APPROVAL DATE 6 August 2002

### STUDY OBJECTIVE:

After the completion of a pilot study (WU# 01-10004E) assessing previous trends in the evaluation of patients having fever in the hospital (nosocomial febrile illness or "NFI") and investigating the clinical outcome of such patients, we developed a system to identify and guide the evaluation of nosocomial febrile illnesses to augment the standard of care among inpatients under the care of the general internal medicine services or subspecialty services within the Department of Medicine at WRAMC. Our direct objectives are to employ this system and assess the diagnostic yield of the initial evaluation of NFI, and assess subsequent mortality, morbidity, and length of hospital stay in this population. We will compare this information with a control population – matched for age and day of admission.

### TECHNICAL APPROACH:

There have been no deviations from the methods stated in the original protocol or the addendum from April 2003.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Updated literature review: There has been no additional pertinent research completed in this area since the time of original protocol completion to our knowledge. A PubMed search using keywords "nosocomial" and "fever" was performed to obtain this information. Study findings to date: Study data is too limited to state any significant findings, although endpoints collected have provided the following information: Study patient data: Average length of stay: 18.12 days. In-house Mortality rate: 1 inpatient death of 12 patients. Control patient data: Average length of stay: 14.95 days. In house mortality rate: 1 inpatient death of 24 control patients. We were unable to calculate other intended study endpoints due to limited data (not all enrolled patients have follow-up data available yet). However, the data provided above is not unexpected. Modifications: The original protocol was modified according to the text provided in the addendum submitted in March 2003, and later approved by the HUC in April 2003. Adverse events: None. Patients withdrawn: None. Enrollment data for study: Study subjects enrolled: 12. Control subjects enrolled: 24. Control patients converted to study patient: 2. Total patients enrolled: 36. Dropouts: 0. The number of subjects enrolled to date at WRAMC is 36. We have enrolled 12 fever patients of an intended number of 100, and have enrolled 24 control patients of an intended 200. There have been no adverse events or unexpected data collected. Although we have been enrolling patients since 8 April 2003, we have only encountered 75% (12 enrollees for fever group to date, while we would have expected 16) of the number of expected candidates to allow us to meet our goal of 100 study patients in one year's time. This is likely due to severe downsizing of the inpatient census during wartime activities. We expect the number of study candidates to vary over time, but expect the number of patients available for enrollment to correlate with inpatient census. Now that the hospital is accepting more inpatients, we anticipate coming closer to our enrollment goals. 100 study patients (and approximately 200 control patients) are needed to meet our statistical requirements in order to provide adequate power to the study. If we are unable to enroll 100 study patients by the time our one-year study period is over, we will likely request an extension of our approved protocol duration.

### CONCLUSIONS

The data collected has been too limited to make any conclusions.

## DETAIL SUMMARY SHEET

**TITLE:** Double-Blinded, Placebo-Controlled, Prospective Randomized Trial Evaluating the Efficacy of Continuous Paravertebral Catheter With Paravertebral Block in Breast Cancer Surgery

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** Buckenmaier, Chester C., LTC MC

**ASSOCIATES:**

**DEPARTMENT:** Surgery

**STATUS:** O

**SERVICE:** Anesthesia-Operative

**INITIAL APPROVAL DATE:** 13 August 2002

### STUDY OBJECTIVE

**Primary:** (1) To compare the degree of pain and nausea associated with continuous paravertebral anesthesia and single injection paravertebral block for breast cancer surgery. (2) To compare the mood state or level of symptom distress following continuous paravertebral anesthesia and single injection paravertebral block for breast cancer surgery. **Secondary:** To compare the time of return to normal activity and full employment after continuous paravertebral anesthesia and single injection paravertebral block for breast cancer surgery.

### TECHNICAL APPROACH

This is a double-blinded, placebo-controlled, prospective, randomized, single center trial comparing single injection paravertebral (PVB) at T3 (with supplementation at T1 and T6) followed by continuous infusion of 0.1% or 0.2% ropivacaine versus normal saline placebo for 48 hours postoperatively in patients undergoing breast cancer surgery. Patients will undergo PVB placement with 0.5% ropivacaine with single shot injections at T1, T3 and T6 for surgical anesthesia. A peripheral nerve catheter will then be threaded at the T3 level. Study participants will be randomly assigned to receive one of three treatment groups for the management of their postoperative pain: (1) 0.1% ropivacaine (2) 0.2% Ropivacaine or (3) placebo. In addition, they will be stratified by procedure (modified radical mastectomy, simple mastectomy, and breast conservation procedure) and body mass index (BMI  $\leq$  30% and BMI  $>$  30.) They will be discharged home after 24 hours with the PVB catheter in place. The infusion will run at a pre-set rate of 10ml/hr for the next 48 hours at which time the patient or family member will remove the catheter.

Data collection will include demographic data; medical, surgical and anesthesia history; stage of cancer; ASA physical status classification; intra-operative factors; dose and duration of narcotic/non-narcotic analgesic use; time to return to regular diet; time to return to activities of daily living and full employment; serial pain and nausea/vomiting score; mood state and level of symptom distress measures, and 30-day operative morbidity. Data collection will take place in person and by phone pre-operatively; twice daily for 72 hours (while catheter is in place); every other day for 96 hours; at patient's follow up appointment (approximately 2 weeks), and at one month.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

To date, there have been no patients enrolled in this study due to lack of personnel to implement the protocol. This manpower shortage was exacerbated by Operation Iraqi Freedom. We are planning to begin enrollment 01 July 2003.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

### CONCLUSIONS

Not applicable.

## DETAIL SUMMARY SHEET

**TITLE:** Electrical Impedance Scanning of Thyroid Nodules Prior to Thyroid Surgery – A Prospective Study

**PRINCIPAL INVESTIGATOR:** Stojadinovic, Alexander MAJ

**DEPARTMENT:** Surgery

**STATUS:** O

**SERVICE:** General Surgery

**INITIAL APPROVAL DATE:** 11 June 2002

**STUDY OBJECTIVE:** There are two main objectives. The first is to evaluate the accuracy of EIS in identifying thyroid malignancy. The second is to characterize the conductivity and capacitance of various thyroid nodules evaluated by electrical impedance scanning (EIS); the analysis will focus on differences between benign and malignant nodules.

**TECHNICAL APPROACH** This is a prospective single arm study of adult patients with thyroid neoplasms scheduled to undergo thyroid resection. This is a feasibility study. The findings of electrical impedance scanning are not used for medical management; therefore, the operative plan is not affected by participation in this protocol. Findings at operation, not EIS results, are the basis on which extent of resection is decided. Exclusion of pregnancy by testing or by history is required prior to inclusion in the study. All patients undergo preoperative assessment with electrical impedance scanning (EIS) using the TransScan TS 2000I™. Operation of this device is very straightforward. The principal investigator has performed all EIS examinations in the General Surgery Clinic. A low-level, biocompatible electrical current, applied via a metal cylinder (base electrode) held in the recumbent patient's hand, flows through the patient's body during the EIS examination. The hand-held TransScan TS 2000I™ probe is applied on the thyroid gland. The matrix of sensors on the probe measures electrical current. The computer calculates tissue-related conductivity and capacitance based on the values of electrical current measured on the skin surface. The recordings of each thyroid lobe are done in a pre-programmed sequence in accordance with the image acquisition technique (frequency range 100-2000 Hz). A high-resolution (16 x 16 sensor array) targeted mode is employed to evaluate the thyroid nodule and gland. Comprehensive thyroid scanning takes five minutes to complete. Tissue-related conductivity and capacitance utilizing the high-resolution targeted mode is calculated utilizing a computer software program. The findings of the EIS are graded on a five-tier level of suspicion scale that has been previously established based on tissue-related conductivity and capacitance. The results of EIS are compared with permanent section histopathology diagnosis that serves as the "gold standard". The patients undergo isthmusectomy, lobectomy and isthmusectomy, or total thyroidectomy as indicated by the primary pathology. The histopathologic diagnosis for all patients is reviewed and confirmed by an attending pathologist. The primary tumor site, radioiodine scan uptake (hot, warm or cold) histologic subtype, size, grade of the tumor, along with extrathyroidal extension of disease, multifocality, and coexistent benign pathology are recorded in the study's secure computerized prospective database.

**PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE** There have been no adverse events. A pilot study evaluating the clinical accuracy of EIS in identifying thyroid cancer was conducted at Hadassah University Hospital, Israel. EIS followed by fine needle aspiration of 37 thyroid nodules was performed detecting 6/7 cases of thyroid cancer in that group of patients. The breast probe, which was used in that study was not optimal for neck scanning, therefore, a smaller probe designed specifically for neck scanning, was developed and will be used in the current study. A total of 31 subjects have been enrolled in this study to date. Twenty-two patients have undergone scheduled thyroidectomy. EIS algorithm performance has been analyzed thus far according to all nodules (n=44) detected and patients with complete data sets (n=22, see table below).

Category	Sensitivity	Specificity	PPV	NPV	Accuracy
Nodules	10/14 (71%)	27/30 (90%)	10/13 (77%)	27/31 (77%)	37/44 (84%)
Patient	7/9 (78%)	11/13 (85%)	7/9 (78%)	11/13 (85%)	18/22 (82%)

**CONCLUSIONS** Electrical impedance scanning of thyroid nodules prior to thyroid surgery demonstrates promising preliminary performance that warrants continued study as planned in this IRB-approved protocol.

## DETAIL SUMMARY SHEET

TITLE: Electrical Impedance Imaging For Early Detection of Breast Cancer in Young Women

PRINCIPAL INVESTIGATOR: Stojadinovic, Alexander MAJ(P) MC

ASSOCIATES: COL Craig Shriver, MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: General Surgery

INITIAL APPROVAL DATE: 11 June 2002

### STUDY OBJECTIVE

The purpose of this study is to evaluate the effectiveness of electrical impedance imaging (EIS) as a breast cancer detection modality for young women.

### TECHNICAL APPROACH

Patients are recruited from those who present to the CBCP at WRAMC or from any primary care service in the Walter Reed Health Care System catchment area. The potential study participant is approached by a health care provider and given details of the study, along with an explanation of the EIS device and measurement procedure. If the patient is willing to discuss the possibility of being a research subject, she is given a consent form. EIS examination is performed only after the woman has signed the informed consent form. This is a prospective single arm study of female military health care beneficiaries age 18-45 years. All patients undergo outpatient assessment with electrical impedance scanning (EIS) using the T-Scan 2000ED™. The T-Scan 2000ED™ consists of a flat screen monitor with a computer mounted on the back. A metal cylinder (held in the woman's hand) is connected to the computer. A low-level electrical signal is transmitted to the cylinder. The electrical circuit is completed when the hand-held scan probe is placed on the woman's breast. The EIS examination requires the placement of a conducting gel (Gamma Gel, used for ultrasound examinations) on the sensor surface of the breast as well as on the metal cylinder use to transmit the electrical signal. Measurements are made with a hand-held probe (detector) nine locations (sectors) on the breast including the nipple. Measurement data for each sector are presented as an image. When an adequate image is obtained, the examiner presses the "record" button on the probe, and the image is recorded. During recording, capacitance and conductivity are measured over seven frequencies (ranging from 100Hz-1MHz). A recording starts in the nipple sector and then follows a pre-set computer-guided sequence around the breast, starting in the upper, outer sector and proceeding from lateral to medial. When recording for the entire breast is completed, a post-processing algorithm in the software is activated. If the measurements for the breast are within the normal range, a green line appears next to the image of the breast; if the measurements are above the normal range, a red line appears next to the image of the breast. It should be noted that the final output of the examination (suspicious [red] / not suspicious [green]) is based on a number computed by the algorithm. The image is only used in this examination to ensure that adequate contact is achieved between the probe and the skin surface. The measurement takes approximately five minutes, after which the gel is removed. The procedure is very simple and virtually risk-free.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 379 and the total enrolled to date at WRAMC is 379. The total number enrolled study-wide is approximately 1,115.

Here is a summary of the initial multi-center experience in abstract format:

First experience with T-Scan for the Early Detection of Breast Cancer in Young Women: Preliminary Results of 1,115 patients taking part in a Multi-center Prospective Trial.

(Alexander Stojadinovic, David Gur, Sarah Lenington, Wende Logan, A. Yeshaya, Scott Fields, Z. Gallimidi, Ron Ginor, Craig D. Shriver/)

**Background:** The standard of care for breast cancer screening in women age > 50 years is mammography. However, for women under 50 years of age, clinical breast exam (CBE) is the accepted standard for screening. CBE-detected cancers are often more advanced than cancers detected with standardized screening modalities, thus requiring more aggressive treatment and accompanied by loss of quality adjusted life years. Breast cancers appear to be more aggressive in younger than older women making early detection of this disease a priority. Our study evaluated the potential for complimenting the CBE with a novel technology, Electrical Impedance Scanning (EIS), in average risk women.

**Aims:** To evaluate the feasibility of EIS as a compliment to CBE for the early detection of breast cancer in young average-risk women.

**Methods:** All women (emphasizing age < 45 years) presenting for screening CBE, mammography, ultrasound (US), or breast biopsy were eligible for study. EIS examination was performed on both breasts using TS2000ED™ (TransScan Medical, Ramsey, NJ). The EIS exam utilizes low-level electrical current instead of ionizing radiation, and takes ~ six minutes to perform. Multiple logistic regression analysis was used to estimate the independent contribution of clinical variables to algorithm performance.

**Results:** Thirty-one cancers were identified among 1,115 women. Seventy-six percent of invasive cancers were non-palpable. Twelve cancers were identified in women age ≤ 45. There were no adverse events and no patient reported discomfort during the TScan exam. Sensitivity and specificity of T-Scan for the target population of women age < 45 was 43% and 94%, respectively. Exogenous estrogen use and menopausal status correlated significantly with algorithm performance (menopausal status:  $t=2.54$ ,  $p=0.01$ ; hormone use:  $t=2.94$ ,  $p=0.003$ ) such that increased false positive rates were identified among postmenopausal women and those taking exogenous hormones. There was no correlation between EIS performance and family history, prior breast cancer, or palpability. The likelihood of having breast cancer was significantly higher for a (+) than (-) EIS screening test. Risk correlated with age: increased likelihood of cancer was 2.3, 3.0, and 4.9 for woman < 50, < 46 and < 40 years of age.

**Conclusion:** EIS is a promising new technology for the early detection of breast cancer and identifies young women at increased risk of having the disease. The positive T-Scan-associated breast cancer risk compares favorably with the relative risk of the various conditions commonly used to justify early breast cancer screening including family history, inherited genetic mutations, and atypical hyperplasia. The ability to detect sub-palpable lesions with high specificity may offer improved early disease detection without excessive anxiety and costs associated with higher false-positive rates. Patient satisfaction as been extremely high as evidenced by the following data on our first 81 patients that underwent the IRB-approved survey:

30% of patients are referred from primary care.

Satisfaction survey (pooled results of 81 consecutive patients\*)

Ethnicity: White 70%, African-American 19%, and Hispanic 6%.

38% subjects knew a young (< age 40) Breast Cancer patient (mean 32, range 15-39 years) 90% regarding screening < 40 as “extremely important” 100% would recommend TScan 2000ED to friend or family.

Overall patient satisfaction (scale 0 to 5) with EIS for breast cancer screening in terms of:

Comfort of the EIS exam	4.93
Speed of the EIS exam	4.98
Reporting of EIS exam results	4.94
Patient education during the EIS exam	4.95
Staff professionalism	5.00

**CONCLUSIONS**

Characteristic	T-Scan 2000 ED	
Noninvasive	√Low risk of harm	No adverse events
Simple to perform	1-2 hrs training	High Specificity 94%
Moderate Sensitivity	43%	
Uniform high quality/repeatability	√Easy objective interpretation	Real-time/binary
Finds Early Breast Ca	Highest Sensitivity for tumors < 1 cm	
Cost effective and widely available	√Acceptable to women	High satisfaction

Our hypothesis is that EIS can detect early stage breast cancers in young women not evident on CBE (the currently accepted standard for screening young women). The target population is one that would otherwise not be followed by imaging. We feel that this screening paradigm will increase awareness of breast cancer and the need to participate in screening. There is no intention to look at EIS as a replacement for standard breast imaging. Preliminary data indicates that EIS has modest sensitivity in women < 40, but it should be emphasized that EIS is intended for women with non-palpable lesions. The purpose of this study is to ascertain and analyse initial data relevant to evaluating the potential of EIS as a screening modality for young women. The ultimate goal is to enable physicians to use an easy, fast, simple and inexpensive examination to identify a high risk group that would not be identified otherwise and follow them with imaging modalities prior to normal screening age. Hence, any cancer found with this approach will be one that would otherwise not be detected until it had grown large enough to be palpable.

This study represents an important step involving adaptation of existing EIS technology for use under novel investigational clinical applications using screening EIS for the early detection of breast cancer in young women. We propose to explore the efficacy of using EIS as an integral part of the screening process...a screening process that is widely recognized as deficient currently when examining younger women with CBE alone during periodic office visits to the gynecologist or the primary care physician. We have found in our initial evaluation of EIS for screening that women think that it is extremely important to screen young women for breast cancer. Our patients are very satisfied with the comfort, safety, rapidity and reporting of the EIS, and would uniformly recommend the examination to a family member or friend. If anything, the success of this novel breast cancer-screening paradigm (EIS + CBE if proven efficacious) will most likely increase awareness and compliance of mammography screening.

The public will gain important knowledge as to whether or not the electrical impedance technology has efficacy when being used as a screening tool for younger women, hence, increasing the chance of early detection in a population that would not have undergone a similar screening otherwise. Every early cancer detected using this approach is potentially an important finding because of the patient's age.

## DETAIL SUMMARY SHEET

TITLE: Three-Dimensional Computed Tomography versus Arteriography for Endovascular Aortic Graft Sizing

KEYWORDS: endovascular, three-dimensional CT, graft sizing

PRINCIPAL INVESTIGATOR: Parker, Mary V MAJ MC

ASSOCIATES: O'Donnell, Sean D COL MC; Gillespie, David LTC MC; Goff, James M LTC MC; Starnes, Benjamin MAJ MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: Peripheral Vascular

INITIAL APPROVAL DATE: 20 November 2001

### STUDY OBJECTIVE

To determine the correlation between measurements made using three-dimensional computed tomography and the standard methods of determining the appropriate size endovascular aortic grafts to use for the repair of infrarenal abdominal aortic aneurysms (two-dimensional computed tomography and arteriography).

To determine the proportion of agreement in the graft size chosen using the two methods of measurement.

### TECHNICAL APPROACH

The patient's pre-operative assessment and operative decision-making will not deviate from the current standard of care. Each patient enrolled in the study will undergo the standard preoperative assessment, including CT scan and arteriogram with or without intravascular ultrasound. The CT performed will be General Electric, 5 mm collimation, 1.5 pitch, 120 mV peak, 280 mA minimum, and one second rotations with helical exposure 30-40 seconds. Nonionic contrast (300cc of iodine per ml) is given intravenously at a rate of 2.5 ml/sec (total dose 120 ml) with a scan delay of 40-45 seconds. The patient is scanned from the dome of the diaphragms to the femoral heads. The reconstruction interval is 2.5 mm. The patient's attending vascular surgeon (observer 1) will determine which endovascular aortic graft to use in the repair based on these studies. The choice of graft size is based on multiple measurements of the aneurysm and aortoiliac arteries (appendix 2). The CT scan will then be reconstructed into three-dimensional images using Preview® Treatment Planning Software (Medical Media Systems, West Lebanon, NH). The three-dimensional images will be measured by an attending vascular surgeon not involved in the particular patient's case (observer 2). Observer 2 will complete the measurement form (appendix 2) and choose a graft based on the results. Observer 1 will be blinded to the 3D images and the results of Observer 2's measurements. Observer 2 will be blinded to the arteriogram and to the graft size chosen by Observer 1. The measurement forms for each patient will be maintained by the primary investigator and compared to determine any difference in the individual measurements, as well as graft size. There have been no modifications in this study since its final approval.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been no new literature published on this subject since the final approval of the project. This study has not been amended or modified. No patients have withdrawn from the study, and there have been no adverse or serious events related to this study. The number of subjects enrolled to the study since last APR at WRAMC is eleven and the total enrolled to date at WRAMC is eleven.

### CONCLUSIONS

Approximately half (11/20) of the proposed enrollment has been completed. The data is being compiled; no results are yet available. Enrollment and data collection are proceeding in accordance with the final approved protocol.

## DETAIL SUMMARY SHEET

TITLE: Pre- and Post-Surgical Evaluation of Gait in Patients With L4/5 or L5/S1 Spondylolysis or Spondylolisthesis

PRINCIPAL INVESTIGATOR: Moquin, Ross CDR MC

ASSOCIATES: Shannon, Steven COL MC, Miller, Barri L PT, Schuyler, Jill MS, Cyhan, Tamara RN

DEPARTMENT: Surgery

STATUS: O

SERVICE: Neurosurgery

INITIAL APPROVAL DATE: 11 December 2001

### STUDY OBJECTIVE

The objective of this study is to compare gait patterns of patients with L4-L5 and L5-S1 spondylolysis/spondylolisthesis pre and post surgery, and with normal controls.

### TECHNICAL APPROACH

Methodology (changes per October addendum): The original study called for the evaluators to be blinded to the subject's diagnosis. Each subject, normal control, and surgical subject would then be tested two times. One test was before surgery. One test was after surgery. The problem with this arrangement is that the subjects who received surgery would have a scar that would be seen by the evaluators placing markers and EMG electrodes. To circumvent this problem, we will have five additional subjects that are scheduled to have another type of back surgery entered into the study as a decoy patient. A different marker set will be used in this analysis. Spherical markers will be placed on specific bilateral anatomic and body landmarks. Due to the marker set being used, after proper marker and electrode placement, a static collection will be done to identify the knee and ankle locations. The ankle and knee markers will then be removed to allow the patient to walk freely. Additional muscle activity is of interest to be studied in this protocol. The following seven muscles will be evaluated bilaterally:

T10 paraspinals	Medial hamstrings	Tibialis anterior
L2 paraspinals	Gluteus maximus	
Rectus femoris	Medial gastrocnemius	

After performing a survey of other gait laboratories, it was found unnecessary and unreliable to perform the maximum manual muscle testing. Instead, we will look at phasic muscle activity.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Recent literature review reveals a number of studies with military relevance. There has been no enrollment to date due to equipment/personnel issues. Consequently, no adverse events and no withdrawals. We have since acquired the necessary personnel that has, in part, prompted the addendum. The equipment issues have been resolved. The following modifications to the study design have been suggested: Observational study, gait, and muscle activity will be assessed in patients with L4/L5 and L5/S1 spondylolysis/spondylolisthesis before and about six months after surgery, or when pain-free or pain-controlled. The protocol previously indicated that the patients would be reassessed at three months. However, after further research and consultation with experts on the recovery process, three months was not adequate to see positive changes in gait. Due to the late start in data collection, the anticipated start date has been adjusted to January 2003. Because of the longer wait after surgery, the expected completion has been adjusted to January 2005. These modifications will cause no increase in risks to the participants. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

Acquiring the necessary Biomedical Engineer signifies major progress towards establishing the lab, which is the essential component to conducting quality research. The recommended modifications represent the culmination of months of trouble-shooting of equipment, additional research, and preparation of required documentation. Until this point, we have been collecting normal data, refining our collection technique, and improving efficiency of collection and analysis. Once the addendum is approved, we will be able to officially begin the study.



## DETAIL SUMMARY SHEET

TITLE: Global Advantage CTA Humeral Head Prosthesis for Treatment of Cuff Tear Arthropathy

PRINCIPAL INVESTIGATOR: Doukas, William C., LTC MC

DEPARTMENT: Orthopaedics and Rehabilitation

STATUS: O

SERVICE: Orthopedics Surgery

INITIAL APPROVAL DATE: 23 October 2001

### STUDY OBJECTIVE

In patients with rotator cuff arthropathy who undergo humeral head replacement with the Global Advantage CTA Humeral Head prosthesis (Depuy Inc., Warsaw, IN, USA) we will:

- 1) Evaluate pain relief from pre to post operatively using a visual analog scale.
- 2) Assess change in range of motion in six degrees of freedom (Flexion/Extension, Internal/External Rotation, Abduction/Adduction) from pre to post operatively.
- 3) Assess change in function as assessed using three methods/criteria.
- 4) Compare the results in regards to change in range of motion and improvement in functional scores with historical data.

### TECHNICAL APPROACH

- 1) Patients who have already had the CTA head prosthesis surgery (retrospectively, five patients) will have a chart review to determine improvement, if any, in range of motion and strength from pre operatively. Various demographic data to include age, sex, hand dominance, and duration of symptoms before surgery will be collected. Patients who are being evaluated retrospectively, except for one, will not have filled out questionnaires, and thus this data will be unavailable to analyze.
- 2) Retrospective patients will also be asked to fill out the Modified American Shoulder and Elbow (MASES) questionnaire, the SF 36 questionnaire, and questions pertaining to the UCLA shoulder rating and Neer Limited Goals Criteria.
- 3) Prospective cases (fifteen patients) pre operatively, will be asked to fill out the MASES questionnaire, the SF36, and assessed for range of motion in six degrees of freedom (Flexion/Extension Internal/External Rotation, Abduction/Adduction), and strength based on the scale outlined under "strength" in the MASES form. Patients will also be assessed on the UCLA shoulder scale, demographic data, outlined in #1 above, will be collected.
- 4) Prospective cases will then be asked to fill out the MASES and SF 36 questionnaire post operatively, and be assessed for the UCLA score at the one and two year follow-up. Success based on Neer's limited goals criteria will be assessed at both one and two year marks. Range of motion will be assessed post operatively at the one year and two-year mark.
- 5) All patients will have the prosthesis surgically placed through a standard deltopectoral approach. Technique for placement is outlined in techniques manual for "Global, Total Shoulder Arthroplasty System" (Depuy Inc., Warsaw, IN, USA).
- 6) All patients will participate in the same postoperative rehabilitation program to include immediate passive pendulum exercises, progressive active assisted, and passive exercises.
- 7) Antero-posterior, Scapular Y, and Axillary view radiographs will be obtained pre operatively and post operatively at one year on all patients.
- 8) Data collected post operative will be compared to pre operative data. We will describe the results of historical studies involving similar shoulder scores, but there will be no statistical comparison between the historical data and our data.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are 10,000 shoulder replacements performed annually in the US for a variety of indications to include arthritis, fracture, and osteonecrosis. It is commonly held that Rotator Cuff deficiency in the presence of glenohumeral osteoarthritis is one of the most challenging clinical situations facing the reconstructive surgeon. Neer et al., in 1982,

described a defective rotator cuff as one of several factors that must be considered during shoulder arthroplasty as these factors can be particularly problematic during the operative and post operative period. The biomechanics of the shoulder joint has been well characterized. The intact rotator cuff stabilizes the humeral head in the glenoid fossa during elevation of the arm. There is on average 3 mm of superior translation of the humeral head in the glenoid fossa during the first 30 degrees of abduction, and an additional 1 mm of superior or inferior excursion occurs with continued elevation. A deficiency in the rotator cuff induces significantly greater humeral head excursion. With a large cuff defect, deltoid and inferior cuff contraction causes articulation of the humeral head with the acromion. The impingement of the rotator cuff against the acromion may also contribute to accelerated loss and insufficiency. This has also been termed a "boutonniere" deformity of the humeral head against the corac-acromial arch. This phenomenon, commonly seen in rotator cuff arthropathy, is believed to induce accelerated humeral head articular destruction, as well as erosion of the acromion and acromioclavicular joint. McCarty et al., in 1981, described the "Milwaukee Shoulder" in four females with radiographic glenohumeral destruction and massive tears of the rotator cuff. These authors had identified collagenolytic and neutral protease activity in the synovial fluid, and, using electron microscopic analysis of synovial tissue found microspheroids of basic calcium-phosphate phase crystals. The theory proposed to explain these phenomena is that a Hydroxyapatite-mineral phase develops in the altered capsule, synovial tissue, or degenerative articular cartilage and releases basic calcium-phosphate-crystal microspheroids, which induce the release of activated enzymes causing destruction of the joint. The origin of the basic calcium-phosphate crystals is not fully elucidated, and whether these crystals are the etiology or the result of arthritis is still yet to be answered.

Neer et al. pointed to nutritional and mechanical causes of accelerated arthritis after rotator cuff tear. In addition to the biomechanical changes described above, Neer and colleagues described the nutritional changes associated with massive rotator cuff tear. Massive cuff defects allow for leakage of synovia, joint fluid from the glenohumeral joint, which decreases both the amount and pressure of synovial fluid needed to provide nutritional support to the chondrocytes of the articular surfaces. This decrease in nutritional support is exacerbated by the decrease in glenohumeral motion secondary to pain and loss of rotator cuff function. What ensues is disuse osteoporosis and loss of articular cartilage, which leads to collapse of subchondral bone. The main goal of treatment of rotator cuff arthropathy is pain relief. Improvements in function though certainly welcome, are usually modest. There have been various described methods of treatment in the literature. Initial reports of treatment of rotator cuff arthropathy with constrained and semi constrained arthroplasty was fraught with dismal results. Complications of the constrained arthroplasty included glenoid fractures, loosening of the glenoid component, component dissociation, prosthetic neck fractures, and dislocations. Stress transfer to the glenoid component lead to early implant loosening in as many as 25% of cases. Re-operation for loosening, implant failure, or instability occurred in up to 50% of cases. Semi constrained arthroplasty designs attempted to resist superior migration of the humeral head by alterations in the shape of the glenoid component. These components, similar to the constrained type, were found to have increased glenoid component loosening and poor restoration of motion. Numerous studies have supported the use of non-constrained total shoulder arthroplasty for providing comfort and functional restoration in patients with end-stage glenohumeral arthritis. Torchia and colleagues reported on their series of 113 total shoulder arthroplasty with the Neer prosthesis between 1975 and 1981. Arthroplasty was performed for osteoarthritis, rheumatoid arthritis, and posttraumatic arthritis. These authors found 93% implant survival at ten years, and 87% after fifteen years. Relief from moderate to severe pain was achieved in 83% of shoulders. Active abduction was achieved improved by an average of 40 degrees to an average of 117 degrees. Evidence of definite radiographic lucency surrounding the glenoid component was seen in 44% of cases. Glenoid loosening was associated with pain. Franklin and colleagues noted in their series a high incidence of glenoid loosening in patients with rotator cuff deficient shoulders. This group hypothesized that the eccentric contact with forces concentrated at the glenoid rim (secondary to the abnormal kinematics of the rotator cuff deficient shoulder) led to loosening and tilting of the prosthetic glenoid, termed the "rocking horse" effect. Bipolar shoulder arthroplasty was conceived in 1975 as a design with an oversized head that may prevent tuberosity impingement on the acromion thus allowing increased abductor lever arm and power, while permitting dispersion of joint contact forces over a larger surface area with contact both at the glenoid and the Coracoacromial arch. This prosthesis would also move the center of shoulder rotator downward to avoid glenoid complications, increase stability, and redistribute stresses to decrease wear. Lee and Niemann reported on fourteen patients who were followed for a mean of 3.3 years in whom bipolar shoulder arthroplasty was performed. These authors reported that in their rheumatoid group, good overall pain relief was attained with an average of postoperative range of motion 79 degrees forward flexion, 66 degrees abduction, and 20 degrees external rotation. The patients in whom the bipolar prosthesis was placed as a reconstructive salvage procedure (after a previous reconstructive procedure) had fair pain relief and

less ROM than the rheumatoid group. Swanson et al. reported on their series of 35 shoulders in 33 patients in whom the bipolar implant shoulder arthroplasty was performed. Of these patients, twenty had severe rheumatoid arthritis, ten had degenerative arthritis, and five had posttraumatic arthritis. Pain relief was reported as good to excellent in 31 shoulders, and postoperative range of motion was on average 71 degrees abduction, 45 degrees extension, 79 degrees flexion, and 28 degrees external rotation. Worland and colleagues reported their series of 33 patients who had bipolar shoulder arthroplasty for the diagnosis of rotator cuff arthropathy. These authors found improvement in function and comfort in all patients with an average increase in active forward flexion of 29 degrees and a gain in active external rotation of 39 degrees. Through this prosthesis design appears promising, especially in offering pain relief, early reports have suggested that it may offer suboptimal improvements in range of motion, and there is evidence of early humeral stem loosening, possible due to the loss of the low-friction interface between the humeral component and cup. The introduction of a large polyethylene-metal interface may also generate more polyethylene wear debris, which can lead to osteolysis. Hemiarthroplasty as a treatment option has been evaluated and reported on. Arntz and associates reported on their experience in treatment of 23 shoulders in 23 patients with disabling pain associated with irreparable tears of the rotator cuff and glenohumeral arthritis. Twelve shoulders underwent standard or oversize Neer II humeral prosthetic replacement without glenoid replacement, eleven shoulders underwent arthrodesis. Criteria for hemiarthroplasty vs. arthrodesis included preservation of passive motion, normal deltoid function, loss of glenohumeral joint surfaces, and sculpturing of the coracoacromial arch. The authors found that active forward elevation improved an average of 44 degrees in the hemiarthroplasty group, and an average of 15 degrees in the arthrodesis group. Both groups reported improvement in comfort level and overall function as assessed pre and post operatively using five activities of daily living. These authors concluded that humeral hemiarthroplasty was the preferred method for managing complex irreparable tears of the rotator cuff with glenohumeral arthritis and a functional deltoid.

Pollock et al. reported on their series of thirty patients with rotator cuff arthropathy who underwent prosthetic replacement. Nineteen patients underwent humeral head replacement alone, and eleven shoulders had total shoulder arthroplasty. Total shoulder arthroplasty and humeral head hemiarthroplasty were found to provide similar results with respect to pain relief, functional improvement, and patient satisfaction. Shoulders with hemiarthroplasty, however, were found to have better active elevation post operatively, and the surgery itself had decreased blood loss, anesthesia time, and operative time. Lohr et al. also found improvements in pain relief in patients undergoing hemiarthroplasty for rotator cuff arthropathy. However, the results were inferior compared to total shoulder arthroplasty. The authors did note higher rates of glenoid loosening in patients undergoing total shoulder arthroplasty.

Field and colleagues reported on their series of sixteen patients with rotator cuff arthropathy who underwent humeral hemiarthroplasty between 1989 and 1992. Neer's "limited goals" criteria were used to assess outcome. Ten patients were rated as successful by Neer's limited goals criteria. Among patients rated as successful, average active forward flexion increased from 60 to 108 degrees, external rotation from 16 to 30 degrees, and internal rotation increased an average of 4 vertebral levels from pre to post operatively. Williams and Rockwood and Zuckerman et al. found similar results in their review of shoulders (21 and 15 respectively) with rotator cuff arthropathy that underwent humeral head hemiarthroplasty. Based on the above studies, many authors agree that when the quality of the deltoid muscle is adequate, and the CA arch is intact, hemiarthroplasty should be the procedure of choice for the shoulder with rotator cuff arthropathy. Worland et al. feel that the bipolar shoulder prosthesis is the prosthesis of choice in this patient population. Some of the above data, especially in regards to pain relief, suggest that the standard humeral hemiarthroplasty may not be ideal, and the problems with the bipolar arthroplasty have been discussed above. Results for the Global Advantage CTA Humeral Head prosthesis for rotator cuff arthropathy have never been published. In addition, evaluation methods and criteria used in the above studies evaluating hemiarthroplasty for rotator cuff arthropathy have not been assessed for their validity, reliability, or responsiveness. Because of this lack of data in the English literature, we propose to examine the Global Advantage CTA humeral head prosthesis in patients with rotator cuff arthropathy with methods that have been found reliable and responsive in the literature as well as by the methods done previously in regards to standard hemiarthroplasties for the purpose of historical comparison, pain medications, and physical therapy.

## CONCLUSIONS

Not submitted.

## DETAIL SUMMARY SHEET

**TITLE:** The Initial Stability of Revision Femoral Stems After Extended Trochanteric Femoral Osteotomy: A Biomechanical Analysis of Distal Stem Design.

**KEYWORDS:** Revision Femoral Stems, Biomechanics, Stem design

**PRINCIPAL INVESTIGATOR:** MAJ Kevin L. Kirk, MC

**ASSOCIATES:** LTC John Xenos, MC, CPT Ronald Lehman, MC and L.D. Timmie Topeleski, Ph.D.

**DEPARTMENT:** Orthopaedics and Rehabilitation

**STATUS:** C

**SERVICE:** Orthopedics Surgery

**INITIAL APPROVAL DATE:** 4 December 2001

### STUDY OBJECTIVE

To determine any significant differences in amount of distal motion between two different femoral stems.

### TECHNICAL APPROACH

Only modification to the original design was elimination of the femoral osteotomy. This was approved under an expedited review.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The biomechanical testing was completed at UMBC- Biomechanics Laboratory. The results demonstrated a statistically significant difference in the amount of micromotion measured when a fluted or cylindrical distal stem design was used.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 12.

### CONCLUSIONS

A significant difference exists in the amount of micromotion when comparing a fluted versus a cylindrical distal stem design. These results will assist hip surgeons in determining the best revision femoral stem to utilize during revision arthroplasty.

## DETAIL SUMMARY SHEET

TITLE: "Bean-Shaped" Foot Treated by Cuneiform/Cuboid Osteotomy: Long-Term Follow-up

KEYWORDS: Clubfoot, bean foot deformity

PRINCIPAL INVESTIGATOR: MAJ Kevin L. Kirk, MC

ASSOCIATES: COL Kathleen McHale, LTC Martha Lenhart

DEPARTMENT: Orthopaedics and Rehabilitation

STATUS: C

SERVICE: Orthopedics Surgery

INITIAL APPROVAL DATE: 4 December 2002

### STUDY OBJECTIVE

To determine the long term functional and clinical follow-up of cuneiform/cuboid osteotomies for the treatment of residual clubfoot deformity.

### TECHNICAL APPROACH (Describe the methodology and note any modifications.)

A clinical follow-up and satisfaction survey were administered to 16 patients who had undergone this procedure at WRAMC.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Opening wedge medial cuneiform and closing wedge cuboid osteotomies were performed on sixteen patients (twenty feet) for residual deformity after clubfoot correction between 1986 and 2001. All patients had prior surgical intervention for clubfoot deformity. Postoperative evaluation was performed to include a clinical examination and x-rays. Each patient completed a modified AOFAS midfoot clinical rating scale and a patient-based outcomes disease specific instrument by Royce, et al. The mean age at operation was 7.0 years (range 2.4 to 13.5 years). The mean length of follow-up was 52.2 months (range 24-189 months). Clinical examination demonstrated acceptable foot position in 15 of 16 patients. None of the x-rays demonstrated significant degenerative changes. The modified AOFAS rating for pain revealed 11/12 patients reported none or mild, occasional pain, 1/12 with moderate pain and none with severe pain. The functional rating scale demonstrated all patients reporting either good or excellent results. The disease specific instrument revealed mean score on the satisfaction survey was 1.5 (1= best possible outcome and 4= worst possible outcome) and 1.9 for function.

The number of subjects enrolled to the study since last APR at WRAMC is 16 and the total enrolled to date at WRAMC is 16. The total number enrolled study-wide is n/a if multi-site study.

### CONCLUSIONS

Combining opening wedge medial cuneiform osteotomy with closing wedge cuboid osteotomy is a simple, direct, and reproducible procedure that addresses both forefoot adductus and midfoot supination in residual clubfoot. The long-term results reliably demonstrate the maintenance of correction of the midfoot and hind foot deformity, good overall function and high patient satisfaction. Our results suggest that this procedure is ideal for improvement of deformity and function in those patients with residual clubfoot who are too old for soft tissue release by itself, too young for a triple arthrodesis, or have too much dysfunction to be temporized with orthotic management.

## DETAIL SUMMARY SHEET

**TITLE:** The Effects of Tibial Malrotation on Tibiotalar Joint Biomechanics of The Medial And Lateral Gutters (facets)

**PRINCIPAL INVESTIGATOR:** Dhawan, Aman CPT MD  
**ASSOCIATES:**

**DEPARTMENT:** Orthopaedics and Rehabilitation  
**SERVICE:** Orthopedics Surgery

**STATUS:** O  
**INITIAL APPROVAL DATE:** 19 March 2002

### STUDY OBJECTIVE

This research study intends to define the changes in tibiotalar joint biomechanics after simulated rotational malunions of the tibia in a cadaveric model. This study differs from that by Svoboda et al in that it examines contact areas in the medial and lateral gutters (facets) of the ankle.

### TECHNICAL APPROACH

**Specimen Preparation:** The model established by Tarr et al has been modified to accommodate analysis of the effects of tibial malrotation. This model is nearly identical to that used by Svoboda et al. Twelve pairs of fresh, unembalmed human cadaveric lower limbs will be harvested at the level of the mid-diaphysis of the tibia and utilized in this investigation. Obtained from the Maryland State Anatomy Board, the specimens will be immediately packaged in double-thickness plastic bags and stored  $-20^{\circ}$  Celsius until time of testing. Specimen age and sex will be recorded. After thawing at room temperature for 24 hours, the specimens will be stripped of all soft tissues except the interosseous membrane and the soft tissues of the ankle and foot. Ligament integrity will be evaluated at this time. Anterior ankle arthrotomies will be performed to facilitate placement of the pressure sensor. Each leg will be mounted into a specially designed load frame in a hydraulic materials testing device (Instron Model 8251) to simulate leg stance with the ankle in neutral position. Load is to be applied from the actuator of the materials tester to the proximal aspect of the tibia potted in a fabricated load adaptor. The foot will be statically mounted to the base of the load frame using pins driven from dorsal to plantar through the first and third metatarsals at the metadiaphyseal level.

**Peak pressure, total load, and contact area measurements:** Pressure measurements will be obtained using the Tekscan I-Scan Adjustable Gain Pressure Measuring System. The system consists of a thin, flexible pressure sensor that outputs data to proprietary Tekscan software via a scanning handle. The pressure sensor (model 4000) is 0.15mm thick and consists of two grids of sensing elements arranged over two 2.8 x 3.3 cm areas. The sensors will be placed in the tibiotalar joint through the anterior arthrotomy and placed into the medial and lateral gutters of the tibiotalar joint. Next, the sensor will be calibrated to the range appropriate for this test...a load of 600 Newtons generated by the material-testing device. Once the sensor is calibrated, the specimen will be tested at 600 Newtons and static pressure distributions recorded by computer. The loads will be maintained for one minute to allow for a stable measurement of load distribution by the sensors. At the completion of the 600 N cycle, the load will be removed and the tibia segment internally rotated 10 degrees using the rotation feature of the materials tester. The previous calibration and testing steps will be repeated for this simulated rotational malunion. This will again be repeated for 20 degrees of internal rotation deformity as well as 10 and 20 degrees of external rotation deformity. Random sequence will be employed to prevent bias and allow for each malunion position to be the initial testing position. With four rotational testing conditions, i.e. internal and external rotation at both 10 degrees and 20 degrees, there are 24 sequences in which to conditions could be administered. By means of a computer program based on random number generation, each specimen was assigned to one of these sequences to reduce bias in the order of testing. Each sensor will be used until it no longer provides reliable data, which occurs as a result of lead breakage and violation of the closed space between the sensor layers. Given the moist nature of cadaveric specimens and the high loads involved, sensor life is estimated as being complete testing of two specimens. Thus, fifteen sensors are expected to be used. At the completion of testing for each of the 24 limbs, the ankle will be

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returned to 0 degrees of rotation and the testing repeated to ensure no irreversible changes occurred to the limb. Should irreversible changes (i.e. ligament damage due to excessive loading) or significant intra-articular pathology (i.e. severe degenerative joint disease or articular cartilage defects) be noted after testing, that specimen will be excluded from data analysis. This determination will be made first by macroscopic observation of the external ligaments and capsule followed by disarticulation of the tibiotalar joint in order to observe the joint contact surfaces and to determine the exact location of the sensor on the talar articular surface.

Adverse events: N/A

Patient confidentiality: N/A

Data Collection: Peak pressure, total load, and contact area will be recorded in the medial and lateral gutters of each of the 24 specimens during neutral and 4 induced malrotations. The data table for each specimen will be as follows:

Specimen #	Medial Gutter			Lateral Gutter		
	Peak Press.	CA*	Total Load	Peak Press.	CA*	Total
Load						
Intact						
10° internal rotation						
20° internal rotation						
10° external rotation						
20° external rotation						

\*Contact Pressure

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The completion of this study has been delayed partially due to time constraints and partially due to the difficulty with placing the sensors reliably in the medial and lateral gutters of the tibia-talar joint.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

CONCLUSIONS

No conclusions have been reached.

## DETAIL SUMMARY SHEET

TITLE: Syndesmosis Fixation – The Biomechanical Effects of Three Vs. Four Cortex Fixation

KEYWORDS: syndesmosis; ankle mortise

PRINCIPAL INVESTIGATOR: COL Kathleen A. McHale MC

ASSOCIATES:

DEPARTMENT: Orthopaedics and Rehabilitation

STATUS: O

SERVICE: Orthopedics Surgery

INITIAL APPROVAL DATE: 18 April 2002

### STUDY OBJECTIVE

Investigate the difference between traditional fixation of three cortices for syndesmosis disruption with modification with four cortices.

### TECHNICAL APPROACH

Produce syndesmosis disruption.

Fix bones with three or four cortices.

Test with Enstron.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

Cadaver study.

### CONCLUSIONS

None at the present time.



## DETAIL SUMMARY SHEET

TITLE: Ulnar Nerve Entrapment – A Randomized Prospective Comparison of Subcutaneous vs. Submuscular Ulnar Nerve Transposition

KEYWORDS:

PRINCIPAL INVESTIGATOR: Farber, Gerald, LTC MC  
ASSOCIATES:

DEPARTMENT: Orthopaedics and Rehabilitation  
SERVICE: Orthopaedic Surgery

STATUS: O  
INITIAL APPROVAL DATE: 25 June 2002

### STUDY OBJECTIVE

To perform a prospective randomized study comparing the outcome of two methods of anterior ulnar nerve transposition, (subcutaneous and submuscular) to determine the optimal procedure to assess the clinical results based on Disability Arm Shoulder Hand (DASH) outcome questionnaire/score, clinical examination, complications, and electrodiagnostic studies (EDS), preoperatively and postoperatively.

### TECHNICAL APPROACH

Study includes a 2-year recruitment phase and a 1-year follow-up phase for a total of 3 years. Board-certified surgeons who routinely perform these operations will perform all procedures. Up to sixty military health care beneficiaries over the age of 18 presenting with the diagnosis of cubital tunnel syndrome will be enrolled at WRAMC. The recruitment phase may be difficult to predict to obtain 60 participants, as the number of patients referred for this problem varies. Additional time for recruitment may be required.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study not approved in time to generate the rest of the FY 03 Detail Summary Sheet.

### CONCLUSIONS

Study not approved in time to generate the rest of the FY 03 Detail Summary Sheet.

## DETAIL SUMMARY SHEET

**TITLE:** Anterior Cruciate Ligament Reconstruction with Gracilis and Semitendinosus Tendons - Comparison between Patients Over 40 Years of Age versus Those Less than 40

**KEYWORDS:** Anterior Cruciate ligament, reconstruction, hamstring autograft

**PRINCIPAL INVESTIGATOR:** Kevin P. Murphy, M.D. LTC/MC/USA

**ASSOCIATES:** Matthew A. Javernick, MD CPT/MC/USA, Ronald A. Lehman, Jr., MD CPT/MC/USA, Brett A. Freedman, MD CPT/MC/USA, William C. Doukas, MD LTC/MC/USA

**DEPARTMENT:** Department of Orthopaedics and Rehabilitation

**STATUS:** O

**SERVICE:** Orthopaedic Surgery

**INITIAL APPROVAL DATE:** 16 July 2002

### STUDY OBJECTIVE

To perform a comparison of the results of patients receiving hamstring reconstruction of the anterior cruciate ligament (ACL) in patients over the age of 40 with patients under the age of 40.

### TECHNICAL APPROACH

After patients consent to a Volunteer Agreement Affidavit (DA Form 5303-R, May 89), we will prospectively study 60 patients between age 40 and 60 who will have ACL reconstruction using the gracilis and semitendinosus tendons and compare them to 60 patients under the age of 40. In each case, the same operating surgeon will perform each operation and utilize the same technique. The preoperative and postoperative rehabilitation will be the same for all patients using an aggressive physical therapy protocol. Each of the patients will be given a series of questionnaires to subjectively assess his/her level of function and perceived pain. The following questionnaires will be used: International Knee Diagnostic Criteria (IKDC) questionnaire, the Visual Analog Scale (V.A.S.), the Lysholm knee scoring scale, Cincinnati Score, and a sheet to annotate their scores on the Military Physical Fitness Test. Obtaining the scores on the Physical Fitness Test (PFT) provides an objective means to analyze the patients' preoperative and postoperative level of function. The PFT is a three-event test that varies by Service. The Army's test consists of two minutes of pushups, two minutes of sit-ups and a two-mile run. The Air Forces performs two minutes of pushup, two minutes of sit-ups and a stationary bicycle test. The Navy performs two minutes of pushups, two minutes of sit-ups and a 1.5-mile run. Finally, the Marine Corps performs chin-ups to muscle failure, two minutes of sit-ups, and a three-mile run. In addition to using the PFT as objective data, we will also perform an objective physical exam as part of the IKDC questionnaire. The PFT scores will be obtained pre-injury, post-injury (but before surgery – if available) and postoperatively. Postoperatively, we will collect PFT scores from every record PFT taken during the two-year follow-up period. The most important aspect of the PFT score for our purposes will be the time on the run. We will review pre- and post-operative run times.

Patients over the age of forty years who are scheduled to undergo ACL reconstruction will be identified from the operating surgeon's database. The comparison group of patients (under age 40) will be developed from the same database to compare postoperative functional parameters between patients undergoing ACL reconstruction under and over the age of 40 years. Namely, we will compare lengths of time to return to full strength and activity, change in PFT run times, and results of the knee assessment tools. Patients in the database will all be operated on by one surgeon. Each of the patients will be required to present their Physical Test scores pre-injury, post-injury and post-operatively. A minimum of two years of follow-up will be obtained. Follow up will be conducted mainly as per the current standard for ACL reconstructions by the performing surgeon. Specifically, patients will be seen 2, 6, 12 and 26 weeks post op by the treating surgeon. For reasons of clinical investigation, research participants will be seen at 1yr and 2 yr follow up to complete long-term examinations. Long term follow up is not specifically the routine currently, but many patients of PI were routinely seen for long term follow up prior to conception of this protocol. Outcome data sheets will be completed at the 6-week, 12 weeks, 6 months, 1 year, and 2 year follow-up appointments. The reason for selection of the two-year point for minimal length of observation is two-fold. First, the standard for tier-one journals in the orthopaedic field is a minimum of two years follow-up for clinical prospective studies. Second, the time for full bio-integration of the

hamstring tendon autograft in ACL reconstructions has been shown to be 4 months to 2 years. Therefore, two years is a natural endpoint for evaluation of early ACL reconstruction outcomes.

Patients will be brought into the physical therapy gym on the same day as their appointment with the surgeon to perform the functional testing and questionnaires (IKDC, Lysholm, Cincinnati, VAS), as indicated on the time schedule below (Figure 1). In addition, we will collect the following data on all of the patients: name, social security number, service, rank, date of birth, surgery date, initial injury date, mechanism of injury, other ligamentous injuries, preoperative Lachman and Pivot Shift (from previous notes), Postoperative-Lachman and Pivot Shift, physical therapy, current level of instability, return to pre-index activity level, complications, occupational and recreational activities, and PFT scores. We will also perform and record the results of a Hop test on these patients. A Hop test is a test designed to test the patient's quadricep strength. Patients are asked to hop on one leg forward 10 feet and then back to the starting point. The time for this task is recorded and compared to preoperative times as well as to the contralateral side. The personal identification information listed above will be collected per the routine of clinical follow-up, namely, this information is automatically printed on their SF-600 forms usually used and kept in our out patient convenience files. The personal data sheets and the questionnaire results will be placed in a research file for each patient. Copies will not be placed in the patient's clinic charts. The personal identifying data on these sheets will be controlled and confidentiality preserved in the similar strictest fashion afforded to all records at the Orthopaedic surgery clinic. At no time will names or personal identifying information, that are included on the data collection tool be made available to any one other than the principal investigator or associate investigators. As data sheets and questionnaires are collected and placed into each patient's research file, one of the investigators will enter the data from these sheets into an Excel spreadsheet. A numerical coding system will be the only identifying data placed on this Excel spreadsheet. A master key linking names to assigned study numbers will be made and kept in a locked area of the research office. All completed data sheets and the Excel spreadsheet will be maintained in the orthopaedic surgery research resident office on the 3<sup>rd</sup> floor of Building One. This office is locked at all times and the records will be kept in a secure filing cabinet until three years after the completion of this project in keeping with the code of federal regulations. At the end of this three-year period, all data collection tools (excluding clinic records), Excel spreadsheets, and the master key will be destroyed.

All patients will be examined by an independent orthopaedic surgeon to minimize the surgeon bias in reporting results. The patients will undergo physical examination to include Lachman, Pivot Shift, and varus-valgus instability. Additional objective data will include radiographs for identification of chondromalacia, functional testing, mean thigh circumference, and bilateral comparison using instrumented ligament arthrometer testing (KT-2000) as described by Daniel et al. The mean thigh circumference will be measured 5 cm proximal to the superior pole of the patella and compared to the opposite, uninjured thigh. An objective KT-1000 arthrometer failure is defined as millimeter difference (MMD) > 5mm. Functional testing will involve single-legged hop, vertical jump, and timed single hops over a 6-meter distance.

The anteroposterior and lateral radiographs of both knees will be obtained standing as well as a skyline patellar radiograph to be evaluated for degenerative changes as described by Cicotti et al. Radiographs are standard of care. Minimum changes include: squaring of the femoral and tibial margins, subchondral sclerosis, minimal to no narrowing of the joint space, and absent osteophyte formation. Moderate changes include: a narrow joint-cartilage space and substantial subchondral sclerosis with formation of osteophytes. Classification of severe changes includes obliteration of the apparent joint space in addition to moderate changes. If the subject is unable to travel to WRAMC, arrangements will be made on an individual basis for a standardized data sheet to be sent to a Board Certified orthopaedic surgeon at a local Military MTF in the subject's proximity. The participation of outside orthopaedic surgeons is solely an administrative and facultative arrangement, made necessary mainly by the high mobility of military patients. All surgeries and primary follow-ups will be conducted at WRAMC by one of the investigators. Plain film radiographs (weight bearing anteroposterior and lateral) will be obtained, as per standard follow-up care, to determine the presence and degree of arthropathy. All radiographs will be interpreted by the PI, and those not taken at WRAMC will be mailed and read by the PI to eliminate interobserver reliability issues. Finally, the subjects will complete a series of standardized knee joint questionnaires (IKDC, Lysholm, Cincinnati, and V.A.S). Ideally, these questionnaires will be administered by one of the investigators at WRAMC. If this is not possible due to the inability of the subject to travel to this location, the PI will administer the questionnaires by telephone to assure they are given in a standardized manner. As outlined in Figure 1 below, these questionnaires will be administered preoperatively and then again at 6 weeks, 12 weeks, 6 months, 12 months, and 24 months postoperatively. All questionnaires will be placed and kept in each patient's research file.

Copies of these questionnaires will not be added to each patient's clinic convenience file. Female subjects will be questioned regarding the possibility of pregnancy. A urine HCG test will be obtained for all patients going to surgery in accordance with WRAMC preoperative protocol. This urine pregnancy test is standard of care and female patients of childbearing age (<55 years old) are not permitted to undergo any procedure that requires anesthesia at WRAMC without first undergoing a urine pregnancy test, unless surgical infertility (i.e. hysterectomy) is formally documented in the patient's chart.

Patients will have the following variables measured/recorded at the following time periods. Standard of Care (SOC) is addressed where applicable in the table. If "SOC" does not follow the "X", then this test at this time period is for research purposes only, and is not standard of care.

Figure 1 Time Schedule for Data Collection

TIME	PREOP	6 Weeks	12 Weeks	6 Months	12 Months	24 Months
PE	X (SOC)	X (SOC)	X (SOC)	X (SOC)	X	X
KT-1000	X			X	X	X
Lysholm	X (SOC)	X (SOC)	X (SOC)	X (SOC)	X	X
Cincinnati	X (SOC)	X (SOC)	X (SOC)	X (SOC)	X	X
IKDC	X (SOC)	X (SOC)	X (SOC)	X (SOC)	X	X
Hop Tests	X(SOC)			X(SOC)	X	X
V.A.S.	X (SOC)	X (SOC)	X (SOC)	X (SOC)	X	X
Data Sheet	X (SOC)			X (SOC)	X	X

(PE – physical examination; KT-1000 – a knee exam assessment device; Lysholm, Cincinnati, IKDC (International Knee Diagnostic Criteria), Hop Tests, V.A.S. (Visual Analog Scale) are all questionnaires regarding knee pain and function)

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There remains very little published in regards to anterior cruciate ligament reconstruction in the over 40 year old population. The only literature that specifically addresses this population focuses on the bone-patella-bone. There have been no published results to PI's knowledge specifically evaluating the autologous hamstring autograft technique that has been proposed here. This project has not formally been initiated yet. The orthopaedic service now has a KT-2000 and enrollment is ready to begin.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

#### CONCLUSIONS

This study will begin to accumulate patients in late summer of 2003. It is anticipated that it will be a successful and a beneficial study to the orthopaedic community.

## DETAIL SUMMARY SHEET

TITLE: Effects of Fracture On 1,25 Dihydroxyvitamin D and Bone Density

KEYWORDS:

PRINCIPAL INVESTIGATOR: Polly, David W.; COL MC, Poth, Merrily, M.D.

ASSOCIATES:

DEPARTMENT: Orthopaedics and Rehabilitation

STATUS: O

SERVICE: Orthopedics Surgery

INITIAL APPROVAL DATE: 17 September 2002

### STUDY OBJECTIVE

The objectives of this study are to determine whether there are changes in vitamin D and its active metabolite after long bone fracture and to examine whether any changes seen in vitamin F are reflected in changes in bone density.

### TECHNICAL APPROACH

Patients with long bone fracture will be followed until fracture healing. Serum levels of 25 hydroxy-vitamin and 1,25 dihydroxy-vitamin D, minerals, and bone enzymes will be measured at each visit to the orthopedic surgery clinic. Bone mineral density will also be determined immediately after the fracture and at the time of fracture healing, if there are no contraindications for this facet of the study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

There have been no recent papers that would relate specifically to this study. NOTE: After approval of this study, and before any study subjects were recruited, the Gulf War, with its subsequent deployments and increased patient load in orthopedic surgery ensued. Because of these logistical issues, no patients have yet been entered into this study. We hope to begin to accrue patients in September of this year, at which time we expect things to be more manageable in the Orthopedic Surgery Department.

### CONCLUSIONS

We continue to be enthusiastic about this study and hope to begin to recruit subjects soon, as noted above.

## DETAIL SUMMARY SHEET

TITLE: Predicting Hearing Aid Microphone Preference in Everyday Listening

KEYWORDS: hearing aids, directional microphones, acoustical variables, everyday listening situations

PRINCIPAL INVESTIGATOR: Walden, Brian E., Ph.D. DAC

ASSOCIATES: Rauna K. Surr, M.S., contractor; Mary T. Cord, M.S., DAC

DEPARTMENT: Surgery

STATUS: C

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 5 February 2002

### STUDY OBJECTIVE

The primary purpose of this study was to determine whether a preference for omnidirectional vs. directional hearing aid microphones in everyday listening situations could be predicted from the acoustic characteristics of the listening environment.

### TECHNICAL APPROACH

This study compared omnidirectional and adaptive directional microphone modes programmed into the GN ReSound Canta750D hearing device. The two microphone modes were compared in a variety of everyday listening situations encountered by the participants over a four-week period. Also, laboratory measures of speech recognition in noise were administered with the devices set in each microphone mode. The devices were fit binaurally according to GN ReSound's preferred fitting algorithm. Participation in the study involved two "pre-trial" periods of two weeks and one week, respectively, during which the initial hearing aid fittings were refined and participants were given practice filling out the *Journal of Hearing Aid Use*. The two pre-trial periods were followed by the four-week trial during which the study field data were obtained. Participants completed a *Journal* on every major active listening situation that was encountered for a total of seven days during the month-long trial.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The only similar study reported in the literature, to date, was also conducted at the Army Audiology and Speech Center (DCI WU #00-2510). The results of that study were published in June 2002 issue of the *Journal of the American Academy of Audiology*, and have been reported previously. Data acquisition has been completed on the current study. Specifically, a total of 1599 descriptions of everyday listening situations were obtained from 17 hearing-impaired participants. An eighteenth subject was enrolled, but his data were unusable because he did not fill out the forms correctly. All major data analyses have been completed. A detailed (internal) lab report has been prepared, which will form the basis for future publications and presentations. There were no adverse reactions to participation in the study and no patients enrolled in the study were subsequently withdrawn. There was no direct benefit to the participants, other than each was offered the opportunity to receive the Canta750D devices from the manufacturer without cost as a result of their participation. All 18 participants elected to do so. The number of subjects enrolled to the study since last APR at WRAMC is 18 and the total enrolled to date at WRAMC is 18.

### CONCLUSIONS

The following major conclusions were justified by the data of this study:

1. Directional microphones work better in the test booth than they do in everyday listening situations.
2. Environmental acoustics often limit the effectiveness of directional microphones in everyday listening.
3. Directional microphones work effectively only when a certain set of environmental conditions exist; specifically, when background noise is present, and the signal source is located in front of and relatively near (<10 ft.) to the listener.
4. Fortunately, this set of conditions is encountered relatively frequently in everyday listening, constituting approximately one-third of all active listening time.
5. The omnidirectional mode is the appropriate default setting for most hearing-impaired patients.

## DETAIL SUMMARY SHEET

TITLE: Relationship Between Laboratory Measures of Directional Advantage and Everyday Success with Directional Microphone Hearing Aids – A Pilot Study

KEYWORDS:

PRINCIPAL INVESTIGATOR: Cord, Mary T. M.A. DAC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: C

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 19 March 2002

### STUDY OBJECTIVE

The primary purpose of this study was to determine how directional microphone benefit, as measured in the laboratory, relates to successful use of directional microphone hearing aids in everyday life.

### TECHNICAL APPROACH

This investigation was designed to determine whether a clinical measure of directional advantage is related to success with directional microphone hearing aids in everyday life. Two groups of participants were recruited: "Successful Users" who reported regular use each microphone mode and "Unsuccessful Users" who had been fitted with switchable omnidirectional/directional microphone hearing aids, but who reported little or no benefit from use of the directional microphone mode. The Hearing in Noise Test was administered to assess speech recognition ability with omnidirectional and directional microphone modes. Directional advantage scores were calculated as the difference between the directional HINT score and the omnidirectional HINT score.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 20 and the total enrolled to date at WRAMC is 20. There have been no adverse events and no patients have withdrawn from the study. Benefit to subjects from being in the study is that subjects were given a hearing test and their hearing aids were checked to make sure they were functioning properly.

### CONCLUSIONS

There appears to be no relationship between laboratory measures of directional advantage and everyday success with directional microphone hearing aids. Six of the ten unsuccessful directional microphone users obtained significant directional advantage in the lab and yet they perceive no benefit from the use of directional microphone in everyday life. Conversely, three of the successful users obtained little or no directional advantage in the laboratory yet they report benefit from use of directional microphones in everyday life. Perhaps for these successful users, reduction of annoying sounds is more important than improved speech comprehension in noise. Compensating for the directional microphones roll-off may be very important for some directional microphones users. Of the ten unsuccessful users, four said directional microphones cut out too much of what they want to hear.

## DETAIL SUMMARY SHEET

TITLE: Reliability and Validity of Otoacoustic-Emission (OAE) Paradigms

KEYWORDS: Otoacoustic emissions

PRINCIPAL INVESTIGATOR: Chandler, David W. COL, MS

ASSOCIATES: Dr. Lynne Marshall, Ph.D., Ms. Linda Westhusin

DEPARTMENT: Surgery

STATUS: O

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 4 June 2002

### STUDY OBJECTIVE

To validate a newly developed evoked otoacoustic emissions (EOAE) instrument to enhance measurement of otoacoustic emissions (OAE).

### TECHNICAL APPROACH

Measurement of OAEs is a routine standard of care audiologic test procedure. Scientists from Naval Submarine Medical Research Laboratory, in conjunction with Mimosa Acoustics, have developed an EOAE instrument to improve measurement of OAEs. This study will utilize this new instrument to measure OAEs of patients with unilateral sensorineural hearing loss during their periodic routine audiologic evaluation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No subjects have been enrolled thus far, pending release of funding for this project by USA Medical Research and Materiel Command (USAMRMC). Subsequently, there have been no adverse events (AE), no update to literature review and study findings, and no amendment or modifications to the research study since the last review. Since USAMRMC has now released funding for this project, enrollment of subjects will begin within the next 45 days. The total number to be enrolled is still projected to be up to 50 military healthcare beneficiaries over the age of  $\geq 18$  years.

### CONCLUSIONS

This project is scheduled to begin by June 2003, and should be completed by September 2003.



## DETAIL SUMMARY SHEET

TITLE: Assessment and Validation of Tongue Fatigue for Speech

PRINCIPAL INVESTIGATOR: Solomon, Nancy P., Ph.D., DAC

ASSOCIATES: Cannard, Kevin LTC, MC; Cord, Mary, Ms.

DEPARTMENT: Surgery

STATUS: O

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 6 August 2002

### STUDY OBJECTIVE

The long-term objectives of this research are to validate a clinical assessment of tongue fatigue and to examine its role in disordered speech. Specifically, this project aims to test a non-aversive, minimal-risk physiologic assessment of tongue fatigue. The second specific aim tests the common clinical assumption that the speech of persons with dysarthria is more susceptible to fatigue than normal.

### TECHNICAL APPROACH

This study involves prospective data collection for between-groups comparisons. Three groups of subjects are included: adults with Parkinson's disease (PD), adults with amyotrophic lateral sclerosis (ALS), and neurologically healthy adults (control). Up to 30 persons in each subject group will be recruited and studied to secure valid data from at least 20 subjects in each group. Data collection sessions include screening procedures (questionnaires, hearing screening, speech, and movement screening), speech recording, tongue and hand function assessment (using the Iowa Oral Performance Instrument), and repetitive speech production tasks ("fatiguing exercises"). One change in the protocol (addendum approved 28 January 2003) is that the dementia screening is being accomplished with the MMSE rather than the Iowa Battery of Mental Decline. This substitution was made to be consistent with the majority of current research studies and clinical practice.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Recent research continues to substantiate the role of fatigue and its devastating impact on quality of life in Parkinson's disease (e.g., Garber, & Friedman, 2003; Herlofson & Larsen, 2003) and ALS (e.g., Lou, Reeves, Benice, & Sexton, 2003). No known research has specifically addressed the role of tongue fatigue in disordered speech. No new results have been published or analyzed from the present protocol that would indicate the need to change the current procedures. Data collection under the present protocol has begun with five normal control subjects. All subjects have provided informed written consent and acknowledgment of receiving the approved HIPAA Authorization Form. No subjects have withdrawn their consent to participate. No results are available at this time. Data recruitment for subjects with disorders has been retarded, in part, because Dr. Cannard, Associate Investigator, and primary referral source for patients with movement disorders, has been deployed to serve in Operation Iraqi Freedom since January/February 2003.

The number of subjects enrolled to the study since last APR at WRAMC is 6 and the total enrolled to date at WRAMC is 6.

### CONCLUSIONS

Subject recruitment and data collection will continue during the next year.

## DETAIL SUMMARY SHEET

TITLE: Discrimination of Temporal Asynchrony Within and Across Sensory Modalities

PRINCIPAL INVESTIGATOR: Grant, Kenneth W., Ph.D. DAC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: O

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 10 September 2002

### STUDY OBJECTIVE

The purpose of this study is to determine the ability of normal-hearing subjects to discriminate changes in temporal synchrony between discrete spectral bands of an audio-alone speech signal (within modality) and between audio and video components of an audio-visual speech signal (across modality). Results of this study will add to our understanding of temporal integration of speech cues across the spectrum for both audio-alone and audio-visual communication settings.

### TECHNICAL APPROACH

Two experiments are planned which use naturally spoken sentence materials presented under audio-alone and audio-visual conditions. For each presentation condition, the speech signal is filtered into four discrete narrow spectral bands. For audio-alone conditions, all four bands are presented in two observation intervals. In one interval, all four spectral bands are presented synchronously, as they would be in normal speech. In the other listening interval, one of the bands is displaced in time to either lead or lag the remaining three bands. The subject's task is to identify which listening interval contained the speech stimulus with the misaligned component. For audio-visual conditions, either the normal, unfiltered speech signal or one of the four discrete spectral bands is presented along with a video movie of a female speaker during speech production. As in the audio-alone experiment, two listening intervals are presented; one with the audio and visual signals in synchrony, and the other with the audio band either leading or lagging the video speech signal. The subject's task is to choose the interval with the misaligned signal. For both audio and audio-visual experiments, the degree of asynchrony is controlled adaptively depending on the subject's responses. Correct responses result in a smaller degree of asynchrony (task gets harder), whereas incorrect responses result in a greater degree of asynchrony (task gets easier). The up-down nature of the adaptive track continues until a criterion number of reversals in the direction of the track is achieved, at which point asynchrony thresholds are determined by computing the geometric mean of the temporal asynchrony values for the last six reversals.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Four subjects have completed the audio-visual experiment. An additional two subjects have been enrolled and have begun testing. Two subjects have been enrolled in the audio-alone experiment and data collection has begun. A report of this work has been submitted to the Auditory Visual Speech Processing (AVSP) workshop to be held in France, 4 September 2003.

The number of subjects enrolled to the study since last APR at WRAMC is 6 and the total enrolled to date at WRAMC is 6. The total number enrolled study-wide is 6, if multi-site study.

### CONCLUSIONS

Preliminary results for the audio-visual experiment show that subjects are fairly sensitive to audio-visual asynchrony when the audio signal leads the visual signal (asynchrony thresholds approximately 30 ms). On the other hand, when the audio signal lags the video signal consistent with normal speech production (where the mouth moves into position prior to any sound production), sensitivity to cross-modal asynchrony is relatively poor (asynchrony thresholds approximately 200 ms).

## DETAIL SUMMARY SHEET

TITLE: Effects of Presentation Level on Recognition of Low and High-Frequency Speech

KEYWORDS: presentation level, high-frequency speech, low-frequency speech

PRINCIPAL INVESTIGATOR: Walter Van Summers Ph.D. DAC

ASSOCIATES: Michelle R. Molis

DEPARTMENT: Surgery

STATUS: O

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 16 April 2002

### STUDY OBJECTIVE

To examine whether the negative effects of high signal presentation levels on speech recognition are similar across the speech bandwidth or if these effects are concentrated primarily in high or low frequency regions.

### TECHNICAL APPROACH

Normally hearing listeners were tested for sentence keyword recognition using lowpass and highpass filtered sentences. In a preliminary task, adaptive tracking was used to determine the lowpass and highpass bandwidths required by each listener for approximately 70% correct keyword recognition at a moderate presentation level. The resulting high and low frequency speech bands were then tested further with sentences presented at the same moderate level and at 10, 20, and 30 dB above this level.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The low frequency band showed about a 7% decrease in keyword recognition as levels increased. Presentation level had a greater effect on the high frequency band with scores decreasing by about 25% with the 30 dB increase in level. The greater influence of presentation level on processing of high frequency speech cues is consistent with both physiological and psychoacoustic results, suggesting that cochlear processing may be more linear (less level-dependent) in apical, low frequency regions than in basal regions tuned to higher frequencies.

The number of subjects enrolled to the study since last APR at WRAMC is 7 and the total enrolled to date at WRAMC is 7.

### CONCLUSIONS

Both low and high frequency speech were more poorly recognized at high presentation levels than at moderate, conversational levels. Level dependent decreases in performance were greater for the high frequency speech materials than for low frequency speech. The large decrease in performance at high presentation levels for high frequency speech may partially explain why listeners with severe high frequency hearing loss often receive little benefit for large amounts of high frequency amplification. That is, the high signal levels required by these listeners clearly tend to reduce the recognition accuracy even in the absence of hearing loss.

## DETAIL SUMMARY SHEET

TITLE: Multiservice Laparoscopic Surgical Training in Pigs (*Sus scrofa domestica*) Using the DaVinci Surgical System

KEYWORDS: Robotic surgery, laparoscopy, telemedicine

PRINCIPAL INVESTIGATOR: Schenkman, Noah S LTC MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: O  
INITIAL APPROVAL DATE: 13 November 2001

### STUDY OBJECTIVE

1. The primary objective of this protocol is to train surgeons in the use of the DaVinci surgical system thus preparing them to safely perform robot-assisted surgery in human patients.
2. As a secondary objective, we hypothesize that use of the DaVinci system is associated with a steep learning curve. We intend to describe the learning curve by measuring times associated with performing basic skills at the beginning and end of the training for each surgeon.

### TECHNICAL APPROACH:

The animal facilities at WRAIR, on the Forest Glen Annex, were used for the protocol. All animals were under the care and handling of the veterinary staff at WRAIR. The animals were anesthetized according to protocol, and a pneumoperitoneum was created with a Verress needle. The daVinci laparoscopic trocars were introduced and the daVinci device was connected to the trocars. Using the daVinci device procedures such as prostatectomy, tubal ligation and reanastomosis, ureteroneocystostomy, ureteroureterostomy, nephrectomy, Nissen fundoplication, enterotomy and repair of bowel injury, and cholecystectomy were performed. The animals were euthanized per protocol at the end of the procedures.

### PRIOR AND CURRENT PROGRESS

The 23 surgeons who participated in Phase 1 of the training protocol (daVinci system training) represented seven surgical subspecialties: cardiothoracic surgery (5 surgeons), gynecology (5 surgeons), general surgery (4 surgeons), urology (3 surgeons), otolaryngology (2 surgeons), plastic surgery (2 surgeons), and neurosurgery (2 surgeons) (Table 1). Of these surgeons, 17 subsequently participated in self-guided practice in a pig model (Phase 2). Three of these 17 surgeons did not record any data and therefore their participation was excluded from the final analysis. The average number of procedures performed by the 14 surgeons from whom data was collected was 5.5. A total of 43 practice operations were performed during Phase 2 of the training—37% were performed by general surgery, 30% by urology, 19% by cardiothoracic surgery, and 14% by gynecology (Table 1). Of these 43 procedures, 11 were performed by single surgeons, 30 by two-surgeon teams, and 2 by three-surgeon teams. The procedures performed included (number in parentheses): cholecystectomy (10), radical prostatectomy (8), IMA take-down (6), tubal anastomosis (6), Nissen fundoplication (3), bowel anastomosis (2), pericardial window (2), cystoureterostomy (2), adrenalectomy (1), cystotomy repair (1), nephrectomy (1), and pyeloplasty (1). The protocol was suspended in January 2002, when the machine was brought to the hospital for clinical use. Currently we are awaiting funding for a second daVinci device to be placed at WRAIR to resume the protocol.

### CONCLUSIONS

This has been a successful training protocol that has resulted in excellent training for the surgeons involved, and allowed us to introduce the daVinci device into clinical use with a greatly shortened learning curve. We are currently preparing a manuscript of our initial experience for publication in the peer reviewed literature. A copy will be submitted to the WRAMC DCI when it is finished.

## DETAIL SUMMARY SHEET

**TITLE:** A Randomized, Double-Blind, Placebo-Controlled, Phase III, Clinical Trial Evaluating DCVax™ Prostate Autologous Dendritic Cells Loaded with Recombinant Prostate Specific Membrane Antigen (rPSMA) for the Treatment of Metastatic Hormone Refractory Prostate Cancer (Trial DC3-HRPC)

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** McLeod, David G., COL MC

**ASSOCIATES:**

**DEPARTMENT:** Surgery

**STATUS:** C

**SERVICE:** Urology

**INITIAL APPROVAL DATE:** 12 February 2002

### STUDY OBJECTIVE

To determine how disease progression, measured by time to event analysis, is affected by the administration of DCVax™-Prostate, autologous dendritic cells (DC) loaded with recombinant prostate specific membrane antigen (rPSMA, Medarex Corporation, Annandale NJ), vs. placebo in metastatic hormone refractory prostate cancer (HRPC) patients. The hypothesis is that administration of DCVax™-Prostate will lengthen the time to event progression relative to placebo.

### TECHNICAL APPROACH

The drug to be used in this study, DCVax™-Prostate, is investigational and will be used under IND number BB-IND 8602, which is held by Northwest Biotherapeutics, Inc. Participation in this study can be discontinued for the following reasons: at the patient's request, at an event that requires discontinuation of treatment, or an unexpected or life-threatening adverse event.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study was closed on 22 October 2002, due to funding difficulties by the sponsor. There were no patients enrolled at this site.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is unavailable, if multi-site study.

### CONCLUSIONS:

This study was closed to enrollment due to lack of funding.

## DETAIL SUMMARY SHEET

TITLE: An Open-Label, Multicenter, Ascending, Single Dose Study Investigating The Pharmacokinetics, Pharmacodynamics, and Safety of FE200486 in Prostate Cancer Patients – Protocol FE200486 CS06

KEYWORDS:

PRINCIPAL INVESTIGATOR: McLeod, David G., COL MC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: O

SERVICE: Urology

INITIAL APPROVAL DATE: 30 July 2002

STUDY OBJECTIVE

To investigate the pharmacological effects of ascending single doses of FE200486 administered subcutaneously to prostate cancer patients in terms of testosterone suppression.

TECHNICAL APPROACH

An open-label, ascending, single dose study in sequential cohorts of patients.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are no recent literature or study findings to report. Amendment 3 has been submitted to DCI and is pending review. This study is currently on hold pending FDA review of the 120mg dosing group's testosterone and LFT data. There is one last dosing group planned for enrollment following FDA review and approval.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 58, if multi-site study.

CONCLUSIONS:

None at this time.

## DETAIL SUMMARY SHEET

TITLE: An Open-Label, Multicenter, Extension Study Investigating The Long-Term Safety and Tolerability of Repeat Doses of FE200486 in Prostate Cancer Patients – Protocol FE200486 CS06A

KEYWORDS:

PRINCIPAL INVESTIGATOR: McLeod, David G., COL MC

ASSOCIATES:

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: O

INITIAL APPROVAL DATE: 30 July 2002

STUDY OBJECTIVE

To investigate the long-term safety and tolerability after repeat doses of FE200486 in prostate cancer patients.

TECHNICAL APPROACH

An open-label, multi-center, extension study with study visits ranging from once every two weeks to once every six weeks.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No recent literature or study findings to report. This study is an extension of FE200486 CS06 in which no patients have been enrolled. Amendment 3 has been sent to DCI and is pending review.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 23, if multi-site study.

CONCLUSIONS:

None at this time.

## DETAIL SUMMARY SHEET

**TITLE:** An Open Label Trial on the Effect of I.V. Zometa 4mg on Bone Mineral Density in Hormone Sensitive Prostate Cancer Patients With Bone Metastasis, Protocol CZOL446EUS24, Novartis Pharmaceutical

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** McLeod, David, COL MC

**DEPARTMENT:** Surgery

**STATUS:** O

**SERVICE:** Urology

**INITIAL APPROVAL DATE:** 13 August 2002

**STUDY OBJECTIVE:**

To determine the effect of 12 months of intravenous Zometa (zoledronic acid) 4mg on bone mineral density (BMD), specifically in the lumbar spine (L2-L4), in prostate cancer patients with a history of metastatic bone disease who are concurrently receiving hormonal therapy.

**TECHNICAL APPROACH**

This is a prospective, open-label, single-arm, multi-center study designed to evaluate bone mineral density, changes in markers of bone remodeling, time to first skeletal related event, and safety in prostate cancer patients with a history of metastatic bone disease who are treated with Zometa 4mg. Patients require hormonal therapy to enroll into this study. They receive a fifteen-minute infusion of Zometa 4mg every three weeks for up to sixteen infusions and have a final safety assessment performed four weeks after the last infusion.

**PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE**

The number of subjects enrolled to the study since last APR at WRAMC is 3 and the total enrolled to date at WRAMC is 3. The total number enrolled study-wide is 250, if multi-site study.

All three patients continue to participate in this study. They have received 10/16 infusions. Adverse events reported at this site include: Rising PSA for which the patient was placed on Casodex 50mg (he is S/P orchiectomy), intermittent tingling in left forearm, thumb and index finger (no action required thus far), worsening anemia (lowering of already abnormal lab values, complaints of fatigue, nausea and stomach pain) all of which are improving with the administration of Procrit 20,000 units weekly and a complaint of a one time episode of hip pain after the first infusion necessitating Percocet for pain relief. The same patient also showed a lowering of his blood calcium levels and was placed on additional calcium supplements and had a worsening of already erythematous nose that was diagnosed as rosacea by a dermatologist.

Four serious adverse events (SAE) were reported by the sponsor: Three from Zometa cancer studies other than this one and one from this study. The SAE reported by another site for this study was for a fatal pulmonary embolism possibly related to Zometa administration. The other SAEs reported were pericarditis (possibly to be related to Zometa) right thigh pain with swelling (downgrade from previous report in 2000 and thought not to be related to Zometa) and suspected epileptic seizures with a follow up report identifying hypocalcemia as the cause of the seizures (event thought to be related to Zometa).

There are no amendments, study findings or literature to report. No patients have been withdrawn from the WR study site.

**CONCLUSIONS:**

None at this time. Study is ongoing.



## DETAIL SUMMARY SHEET

**TITLE:** The Utility of Using Gene-Specific DNA Hypermethylation Detectable in Serum as an Early Detection Molecular Marker of Prostate Cancer

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** Moul, Judd, COL MC

**ASSOCIATES:**

**DEPARTMENT:** Surgery

**SERVICE:** Urology

**STATUS:** O

**INITIAL APPROVAL DATE:** 18 April 2002

**NEW ANNIVERSARY MONTH:** February

### STUDY OBJECTIVE

To examine the utility of the use of gene-specific DNA hypermethylation assays in pre-diagnostic serum samples to improve on current serum markers in the early detection and diagnosis of prostate cancer.

### TECHNICAL APPROACH

This study will be conducted as a nested case-control study utilizing patient specimens from the "Serum Bank for Future Detection of New Prostate Cancer Markers in Serum of Patients with Prostate Cancer, Benign Prostate Conditions, and No Prostate Disease". The cases will include 50 prostate cancer patients with at least one previous cancer-negative core needle biopsy sample available. The controls will include 50 participants with two cancer-negative core needle biopsy samples that remain cancer-free for at least two years after second negative biopsy (if available). Controls will be matched to cases on age, race, serum PSA at initial biopsy, and duration between consecutive biopsies.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study did not receive an approval letter soon enough to generate an annual progress report for FY 03.

### CONCLUSIONS

Study did not receive an approval letter soon enough to generate an annual progress report for FY 03.

## DETAIL SUMMARY SHEET

TITLE: Clinical Study Protocol – FastPack™ FREE PSA Immunoassay

PRINCIPAL INVESTIGATOR: COL Judd W. Moul, MC

ASSOCIATES: Amina Ali

DEPARTMENT: Surgery

STATUS: C

SERVICE: Urology

INITIAL APPROVAL DATE: 23 July 2002

Original Master Study Approval (2801) Anniversary Month: December

New Master Replacement Study (for 2801) (03-28017) Approval Month: February

New Anniversary Month: February

### STUDY OBJECTIVE

To evaluate the FastPack™ Free PSA Immunoassay, which is a paramagnetic particle immunoassay for the in vitro quantitative determination of free prostate-specific antigen (free PSA) in human serum. The FastPack™ Free PSA Immunoassay is designed for use in conjunction with the FastPack™ (total) PSA Immunoassay and the FastPack™ Analyzer System for calculating the ratio of free/total PSA, expressed as a percentage (percent free PSA). The clinical data generated will be used for the initial PMA submission for the FastPack Free PSA Immunoassay to the Food and Drug Administration (FDA). While the FastPack Total PSA Immunoassay has been submitted and is near approval pending additional data, the PMA submission for the FastPack Free PSA Immunoassay is dependent on information learned from this study. This study will demonstrate the safety and effectiveness of the Qualigen FastPack® Free PSA assay for the following:

1. Determine the clinical cut-off value for the percent free/Total PSA for differentiation of prostate cancer and benign prostate conditions in patients with a digital rectal examination (DRE) that is not suspicious for cancer.
2. Determine the positive predictive value (PPV) of prostate cancer associated with the free/Total PSA ration when the DRE is not suspicious for cancer.
3. Determine the number of biopsies that can be eliminated by using the FastPack® Free PSA test.

### TECHNICAL APPROACH

This is a retrospective study that will include up to 123 serum samples from WRAMC. A minimum of 369 serum samples from the other participating sites. The FastPack™ Analyzer System and Sample Dispenser will be set up according to instruction in the operator's manual and the FastPack™ PSA kits will be used according to the instructions. A 2-point calibration will be run at the beginning of the study and test controls on every testing day. Results will be recorded on CRFs. Allow serum samples and controls to equilibrate to ambient temperature prior to testing. Test the total PSA high and low controls and verify that the values are in the specified range before testing any patient samples. Samples should be tested in random order without reference to known Total and Free PSA values or diagnosis. Retain the sample label with the patient ID and the printed test result on CRF 01. The operator will have no information about the sample, other than the patient ID. Record any testing failures in the comment section of the log sheet. After testing is complete at WRAMC, store samples below  $-70^{\circ}$  on the day of testing. Clinical data and frozen samples will be sent to Qualigen in California. Samples will be labeled with the patient study number. No patient names will appear on the labels. Samples will be stored at  $-70^{\circ}$  C and used to retest any questionable or discordant results. Once all data has been reviewed and verified and the PMA is submitted, the samples will be discarded.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are no new literature findings to report. There are no AEs to report. The testing has been completed at WRAMC and samples have been sent to Qualigen. Data is currently being reviewed and verified. The number of subjects enrolled to the study since last APR at WRAMC is 121 and the total enrolled to date at WRAMC is 121. The total number enrolled study-wide is 369, if multi-site study.

CONCLUSIONS None yet.

## DETAIL SUMMARY SHEET

TITLE: Clinical Study Protocol – FastPack™ PSA Immunoassay

KEYWORDS:

PRINCIPAL INVESTIGATOR: COL Judd W. Moul, MC

ASSOCIATES: Amina Ali

DEPARTMENT: Surgery

STATUS: C

SERVICE: Urology

INITIAL APPROVAL DATE: 23 July 2002

Original Master Study Approval (2801) Anniversary Month: December

New Master Replacement Study (for 2801) (03-28017) Approval Month: February

New Anniversary Month: February

### STUDY OBJECTIVE

To evaluate the intended use of the FastPack™ Analyzer System in conjunction with a digital rectal exam (DRE) as an aid in the detection of prostate cancer in men 50 years of age or older.

### TECHNICAL APPROACH

This is a retrospective study that will include up to 200 serum samples. The FastPack™ Analyzer System and Sample Dispenser will be set up according to instruction in the operator's manual and the FastPack™ PSA kits will be used according to the instructions. A 2-point calibration will be run at the beginning of the study and test controls on every testing day. Results will be recorded on CRFs.

Allow serum samples and controls to equilibrate to ambient temperature prior to testing. Test the total PSA high and low controls and verify that the values are in the specified range before testing any patient samples. Patient samples should be tested in random order without reference to known PSA. Record results on CRF and any testing failures in the comments section of the log sheet. After testing is completed, store samples below  $-70^{\circ}\text{C}$  on the day of testing. Frozen samples will be sent to Qualigen after all testing is completed in a manner that retains sample temperature below  $-25^{\circ}$  during shipping. Samples will only be labeled with the patient ID number; no patient names will appear on labels. Samples will be kept until the study and data analysis are complete and approval from the FDA is obtained. Once FDA approval is obtained, the samples will be destroyed. Samples will be sent to Qualigen for the sole purpose of retesting of the FastPack™ if needed. The Hybritech test will not be done at Qualigen. Additionally, all samples will be tested using the Hybritech PSA Test within two weeks of the FastPack™ PSA test.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There are no new literature findings to report. There are no AEs to report. The protocol, as described in the above Technical Approach has been completed. However, data analysis has not been completed and FDA approval has not yet been obtained.

The number of subjects enrolled to the study since last APR at WRAMC is 168 and the total enrolled to date at WRAMC is 168.

### CONCLUSIONS

None yet.

## DETAIL SUMMARY SHEET

**TITLE:** Assessing the Predictive Accuracy of Prostate Cancer Prognostic Factors Using Traditional Statistical Methods and Artificial Neural Networks

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** Moul, Judd W., COL MC  
**ASSOCIATES:**

**DEPARTMENT:** Surgery  
**SERVICE:** Urology

**STATUS:** O  
**INITIAL APPROVAL DATE:** 2 October 2001  
**Anniversary Date:** May

### STUDY OBJECTIVE

The purpose of this study is to assess the accuracy of prostate cancer prognostic factors in predicting response to therapy and post-therapy recurrence using traditional statistical methods and artificial neural networks.

### TECHNICAL APPROACH

A disk containing the data set without identifying any patient confidentiality information (SSN, Last name, First name, Address, for example), but with a unique randomly selected code number, will be supplied to the Collaborator and a CPDR staff from CPDR Headquarters. They will analyze the data in terms of recurrence, cancer-specific, and all-cause mortality. Predictive accuracy will be assessed by the area under the receiver operating characteristic curve. The statistical methods are logistic regression, proportional hazards regression, and artificial neural networks. Logistic regression provides the cumulative probability of the outcome under the assumption that all the hazards in the model are proportional, and the artificial neural network provides the probability of the outcome. The artificial neural network can capture any phenomena, including those that exhibit nonlinearities and complex interactions, to the extent that the phenomena are represented in the data. This model is an exploratory model (prediction model). The accuracy of the model will be evaluated in the following way:

1. We will divide the data set into two subsets, one is used for model establishment and the other is used for validation after the model is established.
2. The parameters used to evaluate the accuracy after data validation will be: Sensitivity of the model, Specificity of the model and Receiving operation curve.
3. With these parameters after model evaluation, we will know the accuracy of the model and make adjustment of the modeling cut points, variables and/or coefficients if necessary.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found.

First model to be explored: Disease Outcome for African American's with equal access to care.

In the multivariate model, adjusting for age, PSA, stage, Gleason score, treatment, rank, and co-morbid conditions, the hazard of death from CaP for African Americans was significantly lower than that of Caucasians. The number of subjects enrolled to the study since last APR at WRAMC is 1467 and the total enrolled to date at WRAMC is 1467. The total number enrolled study-wide is 5502, if multi-site study.

### CONCLUSIONS

African Americans were half as likely to die of prostate cancer as Caucasians. This finding is contrary to our prior research and suggests that racial disparities have complex etiologies. Recent research has pointed to access to care, socioeconomic status and other social factors as major contributions to racial disparities in health. This study supports that view. This study is ongoing.

## DETAIL SUMMARY SHEET

**TITLE:** Statistical Modeling Using Pre-Operative Prognostic Variables in Predicting Extracapsular Extension, Positive Margins, and Outcome After Radical Prostatectomy for Prostatic – Retrospective Study Using the CPRDR Prostate Cancer Database

**PRINCIPAL INVESTIGATOR:** Moul, Judd W., COL MC

**DEPARTMENT:** Surgery

**STATUS:** O

**SERVICE:** Urology

**INITIAL APPROVAL DATE:** 9 October 2001

**Anniversary Date:** May

### STUDY OBJECTIVE

The objective of this study is to perform statistical analysis on a group of patients that have undergone radical prostatectomy for prostate cancer. The outcome of this analysis will establish the important preoperative variables that predict disease-free survival after surgery. These variables will then be used to develop a simple equation to predict outcome after radical prostatectomy, capsular penetration and probability of positive margins.

### TECHNICAL APPROACH

The CPDR database of radical prostatectomies at WRAMC between 1985-2000 will be used. 1,085 patients and their data are currently available. Only those patients that have accurate clinical follow-up and variable data will be included in the study. A separate model that employs the number of positive biopsies in place of clinical stage will be performed. More specifically, we will incorporate the number of biopsies (1-6) positive for cancer instead of the clinical stage category in one of the prediction models. The first model is being developed and is in the concept stage. Data is being gathered at this point. This study is a focus on preoperative information. The purpose of this study is to determine those preoperative variables that significantly affect recurrence after radical prostatectomy and to use them to formulate a relative risk equation. A second goal of this study is to validate the relative risk equation.

### Materials and Methods:

The Center for Prostate Disease Research maintains an Institutional Review Board-approved clinical database. From this database all men who were diagnosed with prostate cancer from January 1988 to January 2002 and who underwent radical prostatectomy were considered for this retrospective analysis. These dates were chosen to select only those patients who were diagnosed with prostate cancer in the PSA era. 1,546 patients met criteria and were included in the analysis. Patients were excluded if they had an incomplete data set or had a diagnostic prostate biopsy consisting of fewer than six cores or more than twelve cores. Any patients who received neo-adjuvant hormone therapy were also excluded. Patients undergoing “salvage prostatectomy” after initial radiation therapy were not included in this study.

These patients were treated at nine different military treatment centers across the United States by multiple surgeons. A second group of patients with a full data set was selected as a validation cohort. This group consisted of patients who were treated and followed by multiple surgeons at the Navy National Medical Center. 93 patients met the same criteria as the study group and were included as the validation group. The PSA distribution between the two groups was very similar as was the percent of positive biopsy cores. The validation cohort had fewer AA males. Percent of biopsies positive for cancer was determined by dividing the number of cores with cancer by the total number of cores taken. PSA recurrence was defined as a PSA value of 0.2 or greater. Preoperative variables were first evaluated for significance using a log rank test. The Cox proportional hazard regression analysis was then used to evaluate the preoperative variables in a multi-variate analysis. In the multivariate analysis the PSA was entered as a sigmoidal transformation. A second Cox model was performed using only the significant factors. Results of this analysis were then used to formulate an equation to calculate relative risk of recurrence. This formula was applied to a validation cohort. Significance was defined as a P value <0.05. Kaplan-Meier disease free survival curves were formulated for the significant variables and the risk groups.

**PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE**

A literature search was performed and no new relevant articles were found.

The Center for Prostate Disease Research includes a database with information on patients from multiple treatment centers. These medical centers provide free of charge medical care to military personnel in an equal access setting. The data from this cohort summarizes the outcomes of a multitude of surgeons and is thus widely applicable. This data confirms the well-recognized trend toward more and more patients with non-palpable disease. In 1998 two cohorts of data from the CPDR were comprised of 38.3% and 42.7% of T1C patients. The two cohorts in this study have 52% and 58% of patients with T1C prostate cancer. Stamey et al has reported T1c groups as high as 71%. This stage migration away from palpable disease has made older prognostic nomograms less useful. Many recent studies have confirmed that clinical stage is no longer a significant factor to predict pathological or clinical outcomes.

Preoperative PSA and biopsy Gleason sum continue to be important predictors of PSA recurrence. In this study, PSA provided the most significant prediction of failure. Race continues to be a concerning factor. Diet, androgen status, genetics, socio-economic status, access to care and cultural bias have all been proposed as explanations for the disparity in incidence and treatment outcomes for African American patients. PSA screening has been associated with an initial increase then subsequent decrease in incidence for both AA and Caucasian men. Men of African descent have a high incidence of prostate cancer across North and South America. Additionally, the incidence in Nigerian men is similar to African American men. These facts give more support to the theory of genetic susceptibility to prostate cancer and less support to diet or environmental causes.

**CONCLUSIONS: Preliminary:**

Biopsy quantification adds significant information to a predictive model of PSA recurrence after radical prostatectomy. Race is an adverse risk factor for PSA recurrence after radical prostatectomy, even in an equal access setting. Statistical modeling can be used to estimate individual patients' risk of recurrence after radical prostatectomy using only preoperative information.

## DETAIL SUMMARY SHEET

TITLE: A Deterministic Computer Model of Prostate Cancer Progression Following Radical Prostatectomy

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: O  
INITIAL APPROVAL DATE: 8 January 2002  
Anniversary Date: May

### STUDY OBJECTIVE

To compare the Net Gain/Loss Years (NGLY-theoretical) using a computer model to the actual Net Gain/Loss in Life Years (NGLY-actual)

### TECHNICAL APPROACH

Anonymous data sets will be sent to New Mexico Health Sciences Center, and a computer model will be run for each data set. The data will be analyzed and compared.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found.

First computer model to be attempted was the PSA doubling time, which is useful to predict death as an outcome. From the CPDR database, 473 men who were followed to death after RP were selected. Of the 473, 116 patients had recurrent disease and adequate PSA data to calculate doubling times. Of the 116, 42 patients died of prostate cancer, 69 died from causes other than prostate cancer.

The number of subjects enrolled to the study since last APR at WRAMC is 152 and the total enrolled to date at WRAMC is 152. The total number enrolled study-wide is 473, if multi-site study.

### CONCLUSIONS:

PSA doubling time model: As expected, PSA doubling times were rapid in this early mortality group. The model proved useful to predict death as an outcome. Even in the face of minimal retained disease and aggressive cancer and in spite of positive margins or PSA recurrence, the study suggests that a majority of men should gain life years over WW after RP. Because of the assumption of minimal retained disease for all patients, the model predictions tend to be conservative.

## DETAIL SUMMARY SHEET

**TITLE:** The Utility of Gene-Specific DNA Hypermethylations Within Diagnostic Sextant Biopsies as an Early Detection Molecular Marker of Prostate Cancer

**PRINCIPAL INVESTIGATOR:** Moul, Judd W., COL MC  
**ASSOCIATES:**

**DEPARTMENT:** Surgery  
**SERVICE:** Urology

**STATUS:** O  
**INITIAL APPROVAL DATE:** 18 April 2002  
**Anniversary Date:** May

### STUDY OBJECTIVE

To examine the utility of the use of gene-specific DNA hypermethylation assays in improving the sensitivity and specificity of core needle biopsy beyond current histopathologic methods in the diagnosis of prostate cancer.

### TECHNICAL APPROACH

DNA extraction and bisulfite modification. DNA will be extracted using the Wizard DNA Isolation Kit (Promega, Madison, WI) following the manufacturer's instructions. Isolated DNA (from 10 -1000 ng) will first be bisulfite modified. Briefly, 1 µg salmon sperm DNA will be added to all samples and then incubated in 0.3 M NaOH for 15 min at 50°C, and mixed with 100 µg of a 5 M bisulfite solution (2.5 M sodium metabisulphite, Merck; 125 mM hydroquinone, Sigma, pH 5.0) and incubated overnight at 50°C, under the exclusion of light. The bisulfite is then removed using the Promega Wizard DNA Cleanup System (Promega Corp, Madison, WI). The reactions are then desulphonated by addition of 3M NaOH to a final concentration of 0.3 M NaOH followed by ethanol precipitation. The samples are then resuspended in 10 µl H<sub>2</sub>O and used for subsequent Taqman reactions.

DNA hypermethylation assays. Determination of hypermethylation by real-time MS-PCR will be assessed using the ABI 7900 (PE Biosystems, Foster City, CA). Quantitation by real-time PCR is considered accurate since it plots the PCR product on a curve as it accumulates at each cycle of the reaction, in contrast to conventional PCR that only displays the final cycle PCR product. Primers and probes are designed specifically to amplify bisulfite-converted sequences in the promoter regions of the GSTP1, E-cadherin, and CD44 genes. For each gene of interest, one set of PCR primers and a hybridization probe designed to bind specifically to methylated sequences spanning the promoter region (including from 3 to 4 individual CpG sites) were constructed. Specificity and quantitation of methylated DNA will be tested by running standards of serial dilutions with known amounts of methylated DNA (from 50 ng to 0.005 ng). The amount of input DNA in each sample will be standardized by including internal reference primers designed to bisulfite-converted β-actin sequences in the region of the gene with no CpG sites. Fifty cycles of PCR will be run for all assays, and the precise quantitation of hypermethylated DNA will be determined by reading the midpoint of the linear portion of the S-shaped real-time curves, called the Ct point or threshold cycle. This refers to the OD level at which the number of cycles it takes for each sample to reach that level of fluorescence. Evaluation of other genes that are prevalently found hypermethylated in prostate cancers such as caveolin-1 are also being considered. The sample size of 50 cases and 50 controls provides over 90% power with an alpha of 0.05 to detect a 40% difference in prevalence of hypermethylation of GSTP1 between cases and controls (assuming a pre-diagnostic biopsy prevalence of 50% of GSTP1 in cases and 10% in controls). The difference in proportions of gene hypermethylation between cases and controls will be evaluated using the Chi-square test. The sensitivity and specificity of GSTP1 hypermethylation in the initial biopsy will be determined.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found. Currently, data is being retrieved and data holes are being filled. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

CONCLUSIONS None at this time.



## DETAIL SUMMARY SHEET

**TITLE:** Evaluation of Gene-Specific DNA Hypermethylation as a Molecular Marker to Predict Risk of Biochemical Recurrence Among Men With Clinically Localized Prostate Cancer Who Undergo Radical Prostatectomy

**PRINCIPAL INVESTIGATOR:** Moul, Judd W., COL MC  
**ASSOCIATES:**

**DEPARTMENT:** Surgery  
**SERVICE:** Urology

**STATUS:** O  
**INITIAL APPROVAL DATE:** 26 May 2002

### STUDY OBJECTIVE

To test whether the presence of gene-specific DNA hypermethylation in radical prostatectomy specimens can improve the prediction of biochemical recurrence and disease progression beyond current histopathologic and clinical parameters among men with clinically localized prostate cancer. We will test a panel of genes shown to be methylated in prostate cancer that are associated with aggressive disease characteristics (e.g., CD44, E-cadherin, endothelin and caveolin 1).

### TECHNICAL APPROACH

DNA extraction and bisulfite modification. DNA will be extracted from the tissue sections using the Wizard DNA Isolation Kit (Promega, Madison, WI) following the manufacturer's instructions. Isolated DNA (from 10 -1000 ng) will first be bisulfite modified. Briefly, 1 µg salmon sperm DNA will be added to all samples and then incubated in 0.3 M NaOH for 15 min at 50°C, and mixed with 100 µg of a 5 M bisulfite solution (2.5 M sodium metabisulphite, Merck; 125 mM hydroquinone, Sigma, pH 5.0) and incubated overnight at 50°C, under the exclusion of light. The bisulfite is then removed using the Promega Wizard DNA Cleanup System (Promega Corp, Madison, WI). The reactions are then desulphonated by addition of 3M NaOH to a final concentration of 0.3 M NaOH followed by ethanol precipitation. The samples are then resuspended in 10 µl H<sub>2</sub>O and used for subsequent Taqman reactions.

DNA hypermethylation assays. Determination of hypermethylation by real-time MS-PCR will be assessed using the ABI 7900 (PE Biosystems, Foster City, CA). Quantitation by real-time PCR is considered accurate since it plots the PCR product on a curve as it accumulates at each cycle of the reaction, in contrast to conventional PCR that only displays the final cycle PCR product. Primers and probes are designed specifically to amplify bisulfite-converted sequences in the promoter regions of the E-cadherin, and CD44 genes. For each gene of interest, one set of PCR primers and a hybridization probe designed to bind specifically to methylated sequences spanning the promoter region (including from 5 to 7 individual CpG sites) were constructed. Specificity and quantitation of methylated DNA will be tested by running standards of serial dilutions with known amounts of methylated DNA (from 50 ng to 0.005 ng). The amount of input DNA in each sample will be standardized by including internal reference primers designed to bisulfite-converted -actin sequences in the region of the gene with no CpG sites. Fifty cycles of PCR will be run for all assays, and the precise quantitation of hypermethylated DNA will be determined by reading the midpoint of the linear portion of the S-shaped real-time curves, called the Ct point or threshold cycle. This refers to the OD level at which the number of cycles it takes for each sample to reach that level of fluorescence. Evaluation of other genes which are prevalently found hypermethylated in prostate cancers such as endothelin and caveolin-1 are also being considered. If new information comes available regarding other genes methylated in prostate cancer that are associated with more aggressive disease characteristics, they will be considered for evaluation in this study.

The sample size of 50 cases and 50 controls provides 80% power with an alpha of 0.05 to detect a 30% difference in prevalence of hypermethylation of CD44 between cases and controls (assuming a prevalence of 70% hypermethylation of CD44 in cases and 40% in controls).

Gene hypermethylation will be measured as binary variables (methylated or unmethylated) in the tumor specimen. The genes will be evaluated individually and combined to determine whether evaluating a panel of genes adds value to prediction of biochemical recurrence. The difference in proportions of gene hypermethylation between cases and controls will be evaluated using the Chi-square test. The association between individual gene hypermethylation and risk of biochemical recurrence will be examined using logistic regression techniques. In addition, we will assess the combined effects of the methylation status of the four genes (CD44, E-cadherin, endothelin, and caveolin-1) as well as other clinical and biochemical covariates (e.g., serum PSA level) using a Cox proportional hazards model. If appropriate data are available, time to biochemical recurrence will be evaluated by survival analysis and Cox proportional hazards regression. Multivariate regression methods will be used to simultaneously adjust for potential confounders.

Exploratory analysis will be conducted to evaluate the association between gene specific hypermethylation and clinical failure (local or metastatic disease recurrence and/or progression). Studies have shown from 30-60% of men who have a biochemical recurrence will develop a clinical recurrence within five years after postoperative rise in serum PSA.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found. Currently, data is being retrieved and data holes are being filled.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

#### CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: Clinical Significance of Post Therapy PSA Detected by Ultra Sensitive Assays in the Follow-Up of Prostate Cancer (CaP)

KEYWORDS:

PRINCIPAL INVESTIGATOR: LCDR John A. Taylor, MC, USNR

ASSOCIATES: COL David G. McLeod, MC, USA; COL Judd W. Moul, MC, USA; MAJ Stacey Koff, MC, USA,

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: O

INITIAL APPROVAL DATE: 4 June 2002

Anniversary Date: May

### STUDY OBJECTIVE

To define the clinical utility of PSA (Prostate Specific Antigen) detected by highly sensitive assays after definitive therapy for CaP.

### TECHNICAL APPROACH

PSA recurrence (The definition of PSA recurrence varies from institution to institution. In this study we will define PSA recurrence as any value post surgery that is equal to or greater than 0.100ng/ml.), clinical recurrence and death from prostate cancer will be primary outcomes. Time from initial PSA to outcome will be evaluated with the semiparametric Cox regression methodology. The highly sensitive PSA values obtained over the course of the follow-up will be treated as time-dependent variables in the Cox analyses. The available computer software (the Cox model in statistical analysis software) can handle all the nonstandard situations that occur in this study such as late entry into the risk set and having PSA measurements taken at irregular intervals. The influence of various functions of the PSA values on outcome will be evaluated. Cox models that control for confounding variables will also be analyzed.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and no new relevant articles were found.

The initial manuscript will be completed this week. There have been no amendments or modifications to the initial study. This study does not involve enrollments. This is a retrospective chart review and there are no adverse events to report.

The number of subjects enrolled to the study since last APR at WRAMC is 264 and the total enrolled to date at WRAMC is 264. The total number enrolled study-wide is N/A, if multi-site study.

### CONCLUSIONS

Our data indicate that a PSA level of 0.06 or less, using the ultrasensitive PSA is associated with disease free survival and that a level of 0.1 is associated with a recurrence, either biochemical or requiring further therapy.

## DETAIL SUMMARY SHEET

TITLE: Prostate Cancer Lifestyle Trial and CPDR Database Comparison

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC

ASSOCIATES:

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: O

INITIAL APPROVAL DATE: 4 June 2002

Anniversary Date: May

### STUDY OBJECTIVE

The Preventive Medicine Research Institute and the University of California San Francisco (the PMRI team) and University of California, San Francisco (UCSF), are currently conducting a clinical trial entitled "Prostate Cancer Lifestyle Trial". The purpose of the UCSF protocol is to determine whether comprehensive lifestyle changes (low-fat, soy-supplemented vegetarian diet, moderate aerobic exercise, stress management, and group support) can influence the course of prostate cancer as measured by prostate specific antigen (PSA). The secondary endpoints of the UCSF study include endorectal MRI (Magnetic Resonance Imaging) and MR spectroscopy (MRS) or transrectal ultrasound (TRUS).

The PMRI team is near completion of their study and is beginning to analyze the data. They are concerned that their control group in the San Francisco Bay Area is not indicative of the general population of men with prostate cancer in "watchful waiting" when it comes to lifestyle change. Specifically, some of the participants have attempted to follow the lifestyle change protocol despite the team's request that they make no lifestyle change for one year. If lifestyle changes do affect PSA, they may not have a true control group for comparison. Therefore, the purpose of this sub-study is to use data from the CPDR database to serve as an additional basis of comparison for the UCSF study.

### TECHNICAL APPROACH

The "Prostate Cancer Lifestyle Trial" approved at UCSF is an invitational, randomized, controlled trial. Approximately 130 men with biopsy-documented prostate cancer were enrolled into this study. The experimental group was asked to make comprehensive lifestyle changes for up to two years. The control group was asked not to make any lifestyle changes. PSA levels were drawn twice at baseline and every three months thereafter in both groups. MRI and MR spectroscopy or TRUS were performed at baseline and after 12 and 24 months in all patients. The outcome measures will be assessed by technicians and physicians masked to group assignment. In addition, measures are taken quarterly for lifestyle and quality of life assessment. After the first two years, study participants who have not undergone conventional treatment are assessed for an additional three years for a total of five years. Dr. Ornish's team is asking for permission to review data from the Center for Prostate Disease Research (CPDR) database because they are concerned that their control group may not be representative of the general population. Also, there is a concern that the control group may have made lifestyle changes that may affect the "watchful waiting" of these gentlemen over time.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search has been performed and there are no new findings to report. 355 patients have been selected for this study at WRAMC. Statistical analysis is ongoing.

### CONCLUSIONS

None yet.

## DETAIL SUMMARY SHEET

TITLE: Assessment of Hormonal Therapy on Survival Benefit of Prostate Cancer and Development of an Optimal Management System for Hormonal Therapy

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: W  
INITIAL APPROVAL DATE: 24 September 2002

### STUDY OBJECTIVE

Study withdrawn...to be resubmitted after substantial modification.

### TECHNICAL APPROACH

Study withdrawn.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn.

### CONCLUSIONS

Study withdrawn.

## DETAIL SUMMARY SHEET

TITLE: Characterization of Novel Immortalized Primary Prostate Cancer Cell Lines

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC

ASSOCIATES:

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: O

INITIAL APPROVAL DATE: 23 July 2002

MASTER PROTOCOL APPROVAL DATE: 21 July 1998

### STUDY OBJECTIVE

The goal of this study is to characterize fully new telomerase-immortalized normal and primary tumor-derived cell lines from sporadic and familial prostate cancer patients. The generation of immortalized, primary prostate cancer cell lines that will accurately reflect the *in situ* characteristics of malignant prostate epithelium is imperative. A set of telomerase-immortalized cells that clearly mimic the primary tumors needs to be developed for the study of prostate cancer progression. For this purpose, we have recently generated a total of twelve telomerase immortalized cell lines: six normal and six primary prostate tumor-derived cell lines. These include two sets of matched normal and malignant prostate tissues from the same patients. Transfection of hTERT into a number of normal cell types has resulted in immortalization of these cells without a converting transformation or significant karyological artifacts. The underlying hypothesis for this study is that primary prostate cells transduced with the gene that prevents senescence will show increased proliferation potential without transformation or karyological alterations, thus making them attractive candidates to study. These novel well-characterized cells derived from patients with sporadic and familial prostate cancer will provide insight into the mechanisms of prostate cancer development and will also provide useful tools to test preventive and therapeutic regimens.

### TECHNICAL APPROACH

- 1) Subculture and subclone eleven telomerase-transduced cells. Subculture the cells for at least fifty passages for verification of the establishment of cell lines. Subclone the cells (about passage 15) and adapt the K-SFM grown cells to DMEM+10% FBS + insulin (5µg/ml) + one medium.
- 2) Characterize immortalized cell lines phenotypically. We can compare various markers between the untransduced cells and hTERT-immortalized cells for determination of similarity. We can also investigate the growth regulatory factors. By combining information from normal immortalized cell lines, we will attempt to identify changes in growth regulation that occur during the malignant progress of prostate cancer.
- 3) Characterize immortalized cell lines at the DNA level by various molecular genetic means. Results of various cytogenetic analyses of the cell lines will be compared. These results will allow the determination of chromosome alterations involved in prostate cancer progression.
- 4) Characterize immortalized cell lines at the RNA level by cDNA microarray for gene profiles and for identification of differentially expressed genes. The cell lines derived from matched tumor and normal tissues from the same patients will be particularly useful for differentially expressed gene study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and there are no new articles to report. There are no AEs to report. The final approval letter is date 16 April 2003 and work has not begun on this protocol. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS:

None at this time.

## DETAIL SUMMARY SHEET

TITLE: Serum Protein Patterns as Potential Diagnostic and Prognostic Biomarkers For Prostate Cancer

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: Urology

INITIAL APPROVAL DATE: 7 May 2002

MASTER PROTOCOL APPROVAL DATE: 21 July 1998

STUDY OBJECTIVE

The goal of this study is to identify serum based diagnostic and prognostic biomarkers for prostate tumor patients utilizing serum samples of patients undergoing radical prostatectomy and normal individuals being archived at the Urology Service of WRAMC (collected under WU#2801). Human serum will be analyzed on the Protein Biology System SELDI mass spectrometer (Ciphergen Biosystems, Freemont, CA).

TECHNICAL APPROACH

Development of Protein Profiles Diagnostic of Prostate Cancer: A training set of 50 normal individuals in a control group and 100 prostatectomy patients in the prostate cancer subject group will be analyzed to generate proteomic spectra. The normal individuals are those who have no evidence of prostate cancer by biopsy. The normal individual will be age matched to the subject group regardless of race. The subject group will be evenly distributed among the different clinical stages of prostate cancer. With the defined CPDR prostate cancer proteomics pattern, 500 masked serum samples will be tested. The 500 samples will include 100 normal controls and 400 sera, which consist of different stages of cancer (200 samples of T2 and 200 samples of T3) and race (150 cases of Africa American, evidence of prostate cancer, and 400 250 Caucasians). Several types of protein chips will be comprehensively tested on a few serum samples to obtain a satisfactory condition for the chip to be used. Currently, several types of chip surface are available, cation exchange for binding to positive charged molecule, anion exchange for binding to negative charged protein, metal affinity for metal binding proteins, and hydrophobic chip. The best chip surface with optimum condition will finally be used. (The best chip surface is defined when the Protein Chip yields consistent, reproducible protein spectra, and is able to distinguish between the control group and the subject group.) Ideally, the crude serum without treatment will be analyzed. However, high abundant albumin and gamma globulin in serum can mask the detection of less abundant protein. It becomes necessary to fractionate serum by ion exchange chromatography. The fractionated serum is then applied to anion exchange protein chip surface or metal binding chip surface. The protein spectra from the training set samples will be analyzed by biomarker recognition software or an algorithm developed with a collaborator yet to be identified. A proteomic pattern will be created to discriminate cancer patients from control individuals.

Optimization and Validation: With the defined CPDR prostate cancer proteomics pattern, 500 masked serum samples will be tested. The 500 samples will include 100 normal controls without individuals in the prostate cancer subject group in different stages of cancer (200 samples of T2 and 200 samples of T3). There will be 150 African Americans and 250 Caucasians in the prostate cancer subject group. A similar ratio will be maintained in the control group. The goal is to achieve at least 80% of specificity for prostate cancer patients.

Development of Protein Profiles Prognostic of Prostate Cancer: The success of the initial experiment will be expanded to the identification of disease related patterns. To reveal a pattern for prediction of recurrence of prostate tumor, a group of patients with no recurrent cancer for at least 5 years will be compared with patients who had recurrent disease within two years post-prostatectomy. A training set of 30 to 50 samples from each group will be applied to protein chip analysis. Similarly, multiple chip surfaces will be tested to identify an optimum condition for the analysis. The protein spectra will be analyzed with biomarker pattern software to create the prognostic pattern. This study will yield a pattern, which may predict the outcome of patients after prostatectomy. Validation of the pattern will be carried out in a larger set of masked cancer serum specimens (400 samples) with 5+ years of follow up. The cancer patients for this analysis are the same as in the Diagnostic Profiling Study. However, patients will be stratified for prostate cancer recurrence and no recurrence after radical prostatectomy.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No new literature findings to report. No amendments or AEs to report. So far, 300 serum samples have been analyzed. The number of subjects enrolled to the study since last APR at WRAMC is 300 and the total enrolled to date at WRAMC is 300.

CONCLUSIONS

None at this point.



## DETAIL SUMMARY SHEET

TITLE: Serum Protein Patterns as Potential Diagnostic and Prognostic Biomarkers For Prostate Cancer

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: O

SERVICE: Urology

INITIAL APPROVAL DATE: 7 May 2002

MASTER PROTOCOL APPROVAL DATE: 21 July 1998

### STUDY OBJECTIVE

The goal of this study is to identify serum based diagnostic and prognostic biomarkers for prostate tumor patients utilizing serum samples of patients undergoing radical prostatectomy and normal individuals being archived at the Urology Service of Walter Reed Army Medical Center (collected under WU#2801). Human serum will be analyzed on the Protein Biology System SELDI mass spectrometer (Ciphergen Biosystems, Fremont, CA).

### TECHNICAL APPROACH

Development of Protein Profiles Diagnostic of Prostate Cancer

A training set of 50 normal individuals in a control group and 100 prostatectomy patients in the prostate cancer subject group will be analyzed to generate proteomic spectra. The normal individuals are those who have no evidence of prostate cancer by biopsy. The normal individual will be age matched to the subject group regardless of race. The subject group will be evenly distributed among the different clinical stages of prostate cancer. With the defined CPDR prostate cancer proteomics pattern, 500 masked serum samples will be tested. The 500 samples will include 100 normal controls without evidence of prostate cancer and 400 sera, which consist of different stages of cancer (200 samples of T2 and 200 samples of T3) and race (150 cases of African American, evidence of prostate cancer, and 400 250 Caucasians). Several types of protein chips will be comprehensively tested on a few serum samples to obtain a satisfactory condition for the chip to be used. Currently, several types of chip surface are available, cation exchange for binding to positive charged molecule, anion exchange for binding to negative charged protein, metal affinity for metal binding proteins, and hydrophobic chip. The best chip surface with optimum condition will finally be used. (The best chip surface is defined when the Protein Chip yields consistent, reproducible protein spectra, and is able to distinguish between the control group and the subject group.) Ideally, the crude serum without treatment will be analyzed. However, high abundant albumin and gamma globulin in serum can mask the detection of less abundant protein. It becomes necessary to fractionate serum by ion exchange chromatography. The fractionated serum is then applied to anion exchange protein chip surface or metal binding chip surface. The protein spectra from the training set samples will be analyzed by biomarker recognition software purchased from commercial source or an algorithm developed with a collaborator yet to be identified. A proteomic pattern will be created to discriminate cancer patients from control individuals.

Optimization and Validation: With the defined CPDR prostate cancer proteomics pattern, 500 masked serum samples will be tested. The 500 samples will include 100 normal controls without individuals in the prostate cancer subject group in different stages of cancer (200 samples of T2 and 200 samples of T3). There will be 150 African Americans and 250 Caucasians in the prostate cancer subject group. A similar ratio will be maintained in the control group. The goal is to achieve at least 80% of specificity for prostate cancer patients. Development of Protein Profiles Prognostic of Prostate Cancer: The success of the initial experiment will be expanded to the identification of disease related patterns. To reveal a pattern for prediction of recurrence of

prostate tumor, a group of patients with no recurrent cancer for at least 5 years will be compared with patients who had recurrent disease within two years post-prostatectomy. A training set of 30 to 50 samples from each group will be applied to protein chip analysis. Similarly, multiple chip surfaces will be tested to identify an optimum condition for the analysis. The protein spectra will be analyzed with biomarker pattern software to create the prognostic pattern. This study will yield a pattern, which may predict the outcome of patients after prostatectomy. Validation of the pattern will be carried out in a larger set of masked cancer serum specimens (400 samples) with 5+ years of follow up. The cancer patients for this analysis are the same as in the Diagnostic Profiling Study. However, patients will be stratified for prostate cancer recurrence and no recurrence after radical prostatectomy.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No new literature findings to report. No amendments or AEs to report.

Proteomic spectra of crude serum were generated using the Ciphergen ProteinChip System and pattern detection was performed using Biomarker Patterns Software. One hundred six patients with CaP and 56 controls were randomly allocated between a training set and a test set. The training set, which consists of 44 cancer patients and 30 controls, was used to build a decision tree algorithm. The test set, which consists of 62 cancer patients and 26 controls, was blindly used to validate the decision tree. Accuracy of classification using the test set was 67% and 42% for the weak cation exchange array (WCX2) and the copper metal affinity capture array (IMAC3-Cu) respectively. Combined spectral data from the WCX2 and IMAC3-Cu arrays generated an algorithm that obtained a sensitivity of 85% and specificity of 85% for the detection of CaP.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 300.

#### CONCLUSIONS

These preliminary findings support recent exciting observations that complex protein profiles have promising potential in early detection of CaP and warrant future studies with streamlined technology. Furthermore, the combined effect of using two array types can greatly enhance the ability of protein profile patterns, suggesting the potential utility of alternative approaches in the evaluation of this new emerging technology.

## DETAIL SUMMARY SHEET

TITLE: Functional Characterization of *HEPSIN* – A Transmembrane Serine Protease in Prostate Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: C

INITIAL APPROVAL DATE: 23 July 2002

Master Approval Date: 21 July 1998

### STUDY OBJECTIVE

The underlying hypothesis driving this proposal is that *HEPSIN* plays a critical role in regulation of cell growth and/or differentiation of CaP cells. Preliminary results of exogenous *HEPSIN* expression in metastatic CaP cells PC-3, showed significant growth inhibitory effects. This new finding in conjunction with observations of decreased *HEPSIN* expression in metastatic CaP, led us to suggest that *HEPSIN* negatively regulates cell growth and or metastasis- related biologic functions. The major objective of this study is to discern the functions of *HEPSIN* in primary and metastatic cancer cells and normal prostate epithelial cells.

### TECHNICAL APPROACH

Metastatic CaP cells (PC-3 and LNCaP), immortalized normal prostate cells (MLC- SV40) and immortalized primary CaP cells (CPDR 8) will be used for creating stable transfectants of *HEPSIN* expression vector, which will be analyzed in various cell biologic assays of cell proliferation, apoptosis, cell invasion, and angiogenesis. Study of gene silencing will be done in LNCaP cells. RNA from the transfectants will be used for microarray experiments to analyze pathways regulated by *HEPSIN*. LCM-derived RNA from radical prostatectomy patients will be used for *HEPSIN* expression by TaqMan/quantitative RT-PCR assay. Using an anti-*HEPSIN* antibody, *HEPSIN* expression will be analyzed on tissue microarrays containing tissues from 500 CaP patients.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Expression of *HEPSIN*, a type II transmembrane serine protease in prostate cancer (CaP) has been highlighted by several studies analyzing CaP-specific gene expression alterations by cDNA microarray. Evaluations of the biological functions of *HEPSIN* in CaP cells are warranted for better assessment of its utility as a biomarker and or therapeutic target. In stable clones of PC-3/*HEPSIN* transfectants, there was a dramatic reduction in the cell growth, cell invasion, and soft agar colony formation. A higher proportion of PC-3/hepsin cells were in the G2-M phase of the cell cycle, and there was also an increase in the cell population undergoing apoptosis. Preliminary analysis of *HEPSIN* transfections into LNCaP and DUI145 cells further revealed cell growth-inhibitory effects. These results underscore that exogenous Hepsin expression negatively regulated cell consequence of *HEPSIN* overexpression in primary CaP remains to be determined, the negative cell growth regulator effects of Hepsin in metastatic CaP cells reported here have unraveled possible cellular and molecular mechanisms underlying observation that link decreased loss of Hepsin expression with poor prognosis of CaP.

Dr. Srikantan has decided not to use human tissue for this protocol. Tissue has not and will not be pulled for this study from WU# 2871-98 "Creation of a Tissue Library for the Molecular Biologic Study of Patients with Prostate Cancer". This study is closed. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. There are no adverse events to report.

### CONCLUSIONS:

None.

## DETAIL SUMMARY SHEET

TITLE: Probing Mechanisms of p53 Regulation of Maspin Expression in Prostate Cancer Cells

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC

ASSOCIATES:

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: O

INITIAL APPROVAL DATE: 23 July 2002

Master Approval Date: 21 July 1998

### STUDY OBJECTIVE

We hypothesize that down-regulation of Maspin expression contributes to prostate tumorigenesis. P53 and AR signaling play critical roles in regulation of Maspin expression.

### TECHNICAL APPROACH

Induction of Maspin expression will be assessed in prostate tumor cells containing functional or deficient p53 following exposure to various DNA damage agents and radiation. We will evaluate the effect of Maspin expression on the p53-mediated cellular response, cell growth arrest, apoptosis and radiation sensitivity. Molecular changes induced by Maspin expression will be evaluated by cDNA microarray in prostate tumor cells. We will analyze if androgen ablation-induced Maspin expression results from the activation of p53. Immunohistochemical staining of Maspin in prostate tumors will further determine whether Maspin can be a diagnostic, prognostic or therapeutic marker for prostate cancer patients.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A literature search was performed and there is nothing new to report. There are no AEs to report.

Comprehensive evaluation of Maspin expression profile in multiple tumor foci from whole mounted prostate specimens of prostate cancer patients revealed absence of Maspin expression in a significant fraction (63%). However, Maspin expression is significantly higher in tumor specimens (92%) of patients treated with neoadjuvant androgen ablation therapy before radical prostatectomy. LNCaP cells cultured in androgen-depleted medium show induction of Maspin promoter activity in a promoter luciferase reporter assay. In addition, Maspin expression is increased after castration in LNCaP prostate cancer cells derived tumors in nude mice.

The number of subjects enrolled to the study since last APR at WRAMC is 97 and the total enrolled to date at WRAMC is 97.

### CONCLUSIONS

Conclusions at this time: Maspin expression is frequently absent in primary prostate cancers. Up-regulation of Maspin in response to androgen ablation strongly suggests a physiological role of Maspin in growth inhibition and/or apoptosis of prostate cancer cells during androgen ablation.

## DETAIL SUMMARY SHEET

TITLE: PMEPA1 – A Prostate Abundant Androgen Regulated Gene – Evaluation of Expression and Function in Prostate cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: W  
INITIAL APPROVAL DATE: 10 September 2002

### STUDY OBJECTIVE

Study withdrawn.

### TECHNICAL APPROACH

Study withdrawn.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn.

### CONCLUSIONS

Study withdrawn.

Report Date: FY03

Work Unit # 02-29001

## DETAIL SUMMARY SHEET

TITLE: Breast Reduction in Physically Active Women: Descriptive Report of Active Duty Army Soldiers

KEYWORDS:

PRINCIPAL INVESTIGATOR: Jorgenson, Daniel S. COL MC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: W

SERVICE: Plastic Surgery

INITIAL APPROVAL DATE: 19 March 2002

### STUDY OBJECTIVE

Study was withdrawn.

### TECHNICAL APPROACH

Study was withdrawn.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study was withdrawn.

### CONCLUSIONS

Study was withdrawn.

## DETAIL SUMMARY SHEET

TITLE: Mentor Adjunctive Study For Silicone Gel-Filled Mammary Prostheses

PRINCIPAL INVESTIGATOR: Jorgenson, Daniel S., COL MC  
ASSOCIATES:

DEPARTMENT: Surgery

STATUS: O

SERVICE: Plastic and Reconstructive Surgery

INITIAL APPROVAL DATE: 16 July 2002

### STUDY OBJECTIVE

The objectives of this study are to gather safety data regarding short term, post-implant events and complications needed to support Pre-Market Approval (PMA) submissions for Mentor Silicone Gel-Filled Mammary Prostheses and to maintain a comprehensive record of the patient's ongoing medical history. The FDA has placed the devices in a regulatory category as a Class III device, pursuant to the Medical Device Amendments to the Federal Food and Drug Act effective May of 1976. For devices in this class, FDA requires certain clinical data regarding the risks associated with mammary prostheses. Due to several issues surrounding possible risks of silicone gel-filled implants, the FDA has mandated specific clinical study requirements to further assess possible risks and complications of silicone devices. Clinical data collected via this study will supplement data that will be collected in more extensive core studies for breast reconstruction and augmentation procedures.

The primary objective is safety assessment. Data collected during this study will supply risk and complication data with regard to short-term use of silicone implants. This assessment will include the incidence of capsular contracture, occurrence of infection and seroma, as well as implant rupture rates. Both smooth and textured surface implants are available for use in this study. Textured surface implants were originally designed to reduce the chance of capsular contracture. Some studies with small numbers of women suggest that surface texturing reduces the chance of severe capsular contracture, but studies of a large number of women with saline-filled implants show no difference in the likelihood of developing capsular contracture with textured implants compared to smooth surface implants (see FDA website: <http://www.fda.gov/crdh/breastimplants/biissues>). WRAMC now has a comprehensive breast care center and on average sees 150 breast cancer patients per year. Many of these are referred to the plastic surgery clinic for a discussion of their reconstructive options. Participation in this study would, in addition to being helpful in gathering clinical information, expand those options.

### TECHNICAL APPROACH

This study provides open-label use of the Mentor Silicone Gel-Filled Mammary Prostheses while gathering safety data to support FDA requirements for Pre-Market Approval (PMA) applications subsequent to the 1976 enactment of the Medical Device Amendments. This study at WRAMC will use two different implants, as per the Mentor Adjunct Study Protocol: The Siltex® and Smooth-Surface Low-Bleed Gel-Filled Mammary Prostheses (which is filled with silicone gel) and the Becker Expander/Mammary Prostheses (which has a silicone gel-filled outer lumen and a saline filled inner lumen). Board certified surgeons will perform the breast implant surgery. The surgeons will select the implant used based on patient body habitus and available tissue for adequate coverage of the implant. Subjects will be followed for sixty months following the procedure for study purposes. Pregnancy will be ruled out by performing a urinary HCG lab test. Patients who decline to be part of the Mentor Protocol but undergo reconstruction will be followed in our clinic as we routinely follow these patients. For example, a TRAM flap reconstructed patient will not be part of this protocol, but will be followed up on a scheduled basis post operatively.

Standard of care for prosthetic breast reconstruction at WRAMC usually involves an overnight stay with follow-up initially in 5-7 days, and then two weeks later. In the case of tissue expansion, after sufficient

Work Unit # 02-29002 [*Continued*]

healing, the patient will be followed up weekly for expansion. Once expansion is complete, follow-up is every 3-6 months for two years, and then indefinitely on an annual basis. If immediately reconstructed with a permanent implant after the second postop visit, follow-up is every 3-6 months for two years, and then indefinitely on an annual basis. If a WRAMC patient declines to be part of the Mentor Registry, we will maintain contact with her through the Walter Reed Plastic Surgery Clinic. The patient will be asked to provide the clinic with her new address any time she moves.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The sole modification to date is the inclusion of HIPAA Privacy Rule Authorization Form. Form was reviewed and approved by DCI 7 April 2003. The number of subjects enrolled to the study since last APR at WRAMC is 6 and the total enrolled to date at WRAMC is 6. The total number enrolled study-wide is 60,000, if multi-site study.

CONCLUSIONS

It is too early in this study to draw any meaningful conclusions.



## DETAIL SUMMARY SHEET

TITLE: Oropharyngeal Decontamination for the Prevention of Ventilator Associated Pneumonia with Chlorhexidine Oral Rinse

PRINCIPAL INVESTIGATOR: Ramage, Anthony S. MAJ MC

ASSOCIATES: Jackson, William L. CPT MC; Fitzpatrick, Thomas COL MC

DEPARTMENT: Surgery

STATUS: O

SERVICE: Critical Care

INITIAL APPROVAL DATE: 23 October 2001

### STUDY OBJECTIVE

To evaluate the effectiveness of oral decontamination using chlorhexidine (CHX) gluconate oral rinse for the prevention of ventilator associated pneumonia (VAP) in medical and surgical ICU patients.

### TECHNICAL APPROACH

Beginning on the day of enrollment, or on the day mechanical ventilation is initiated, chlorhexidine gluconate 0.12% oral rinse, or placebo, will be applied to patient's oral cavities following routine oral care. A foam swab will be soaked with chlorhexidine rinse and applied to patient's teeth, gums, tongue, buccal mucosa, and posterior pharynx. Enough CHX rinse should be applied as to fully cover these surfaces, but not so much as to risk aspiration. Approximately 15-30 cc of CHX will be used per application. Daily tooth brushing with foam swabs soaked in a bicarbonate solution with peroxide is standard oral care in the ICU. These patients will all be intubated with an endotracheal tube that has a balloon placed in the trachea. The balloon prevents large volume aspiration. The swabs are attached to continuous suction, and aspiration is highly unlikely. The patients may experience some coughing or associated gagging with the procedure, but not more than would be normally expected from routine oral care. The chlorhexidine will be allowed to sit on these surfaces for 15-30 seconds before being suctioned off by routine oral suction equipment. Placebo will contain the same base solution as CHX oral rinse. Patients will continue to receive routine oral care followed by twice-daily 15-30 second applications of chlorhexidine oral rinse or placebo. Treatment will continue as long as the patient remains mechanically ventilated. The intensive care physicians will dictate all other medical interventions. Patients will be monitored daily for VAP. VAP will be defined by the Centers for Disease Control (CDC) definition and includes a new or progressing and persistent infiltrate on chest radiograph and at least one of the following: fever ( $>38.3^{\circ}\text{C}$ ), leukocytosis or purulent tracheal secretions. Persistence of an infiltrate is defined as having the infiltrate radiographically present for at least 72 hours. Fever is defined as an increase in the core temperature =  $1^{\circ}\text{C}$  and  $>38.3^{\circ}\text{C}$ . Leukocytosis is defined as an increase of 25% or more of the circulating leukocytes. Purulent tracheal secretions will be defined as abundant neutrophils ( $>25$ ) per high power field on gram's stain. The surveillance for VAP is standard care in the ICU and is unaltered by this study. The ICU physicians taking care of the patient will dictate the use of systemic antibiotics for the treatment of suspected VAP. Because of variability in physician practice regarding weaning from mechanical ventilation the Walter Reed weaning protocol – a standardized protocol routinely used in the MICU will be applied to all enrolled patients at Walter Reed.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There has been no progress to date on this protocol. The requirement that surrogate consent be obtained from a medical health care power of attorney (HCPOA) and not just a next of kin significantly hampers this research effort. Every potential subject that has been approached has not had a pre-existing medical power of attorney. As a result, zero patients have been enrolled. The project lost all momentum after a minimum of thirty subjects were ineligible because of this requirement.

### CONCLUSIONS

This research is in jeopardy. At the present time, PI is re-focusing the effort to enroll patients prior to requiring mechanical ventilation, as stated in the protocol. If this fails to produce some subjects in the following months, I may be forced to convert this to a quality improvement project.

## DETAIL SUMMARY SHEET

TITLE: Surgical Correction of the Incompetent Nasal Valve – A Rhinometric Analysis

KEYWORDS: nasal valve, rhinometry

PRINCIPAL INVESTIGATOR: Bentley, Anthony, LTC MC

ASSOCIATES:

DEPARTMENT: Surgery

SERVICE: Otolaryngology

STATUS: O

INITIAL APPROVAL DATE: 9 October 2001

### STUDY OBJECTIVE

To ascertain, quantify, and compare the efficacy of different approaches to treating nasal valve collapse. These include butterfly grafting, spreader grafts, and flaring sutures. Rhinometry will be used to provide data for comparison.

### TECHNICAL APPROACH

No modifications have been made. The nasal valve will be approached via an open rhinoplasty technique, and a butterfly graft, spreader graft, and flaring sutures will be applied to each head. Rhinometry will be obtained following each approach. This will be repeated on each of ten heads.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

### CONCLUSIONS

This study is a cadaveric study, approved for ten heads. This study will be conducted upon the return of Dr. Bentley from a rotation in California.

## DETAIL SUMMARY SHEET

TITLE: Mighty Mitomycin – Novel Use of Topical Mytomycin to Prevent Middle Ear Adhesions in An Animal Model

KEYWORDS:

PRINCIPAL INVESTIGATOR: Doolittle, Andrew CPT MC  
ASSOCIATES:

DEPARTMENT: Surgery

STATUS: O with no approval letter

SERVICE: Otolaryngology – Head & Neck Surgery INITIAL APPROVAL DATE: 8 January 2002

### STUDY OBJECTIVE

This study does not yet have budget approval.

### TECHNICAL APPROACH

This study does not yet have budget approval.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study does not yet have budget approval.

### CONCLUSIONS

This study does not yet have budget approval.

## DETAIL SUMMARY SHEET

TITLE: Investigation of Nasal Obstruction on the Outcome of Home-Based and Hospital-Based Evaluations of Obstructive Sleep Apnea and Snoring

KEYWORDS:

PRINCIPAL INVESTIGATOR: Pazos, George A. LCDR MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Otolaryngology – Head & Neck

STATUS: T  
INITIAL APPROVAL DATE: 15 January 2002

### STUDY OBJECTIVE

Study terminated.

### TECHNICAL APPROACH

Study terminated.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study terminated.

### CONCLUSIONS

Study terminated.

## DETAIL SUMMARY SHEET

**TITLE:** The Use of Intraoperative Rapid Parathyroid Hormone Assay in Predicting Postoperative Hypocalcemia Following Total/Near-Total Thyroidectomy

**PRINCIPLE INVESTIGATOR:** McLeod, Ian K. CPT MC

**ASSOCIATES:** Arciero, Cletus A. MAJ MC; Shriver, Craig COL MC; Peoples, George LTC MC; Stojadinovic, Alex MAJ MC; Noordzij, Pieter MAJ MC; Langley, Roy MAJ MC; Bernet, Victor LTC MC; Howard, Robin

**DEPARTMENT:** Surgery

**STATUS:** O

**SERVICE:** Otolaryngology – Head and Neck

**INITIAL APPROVAL DATE:** 29 January 2002

**SERVICE:** General Surgery

### STUDY OBJECTIVES:

- 1) Does the fall in intraoperative rapid PTH levels immediately following total thyroidectomy correlate with a fall in postoperative serum calcium levels?
- 2) What degree of change in rapid PTH level, or what absolute level of rapid PTH, predicts postoperative hypocalcemia?
- 3) Are changes in intraoperative rapid PTH levels immediately following total thyroidectomy associated with the number of parathyroid glands inadvertently removed?
- 4) Do rapid PTH values correlate with intact PTH values?
- 5) Do ionized calcium levels correlate with serum calcium values?

### TECHNICAL APPROACH:

All patients presenting to the General Surgery or Otolaryngology-Head and Neck Surgery Clinics for total or near total thyroidectomy are screened to see if they meet criteria for enrollment in this study, as outlined in our protocol. Once enrolled and the proper consent have been obtained, patients then undergo routine preoperative evaluation and workup. The patients undergo standard surgical therapy for their particular disease process; the only modification is a series of blood draws before, during and after their procedure. The key laboratory study is that of the rapid PTH assay. This assay is performed utilizing an Immunolite Immunoassay System that can determine parathyroid hormone levels in approximately 15 minutes. The surgeons are blinded to the intraoperative values and patients are recovered postoperatively in a routine manner. In addition to various laboratory studies, all postoperative events, especially any events of hypocalcemia, are recorded. There have been no modifications to our technical approach as it has been delineated in our original proposal.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE:

A total of 27 patients were eligible for the protocol and have been enrolled in the study to date. This group consisted of 5 males and 22 females. Total thyroidectomy was carried out in 25 patients, while 2 underwent completion thyroidectomy. The presenting diagnosis was cancer in 7 patients (1 medullary carcinoma, 5 papillary carcinoma and 1 follicular carcinoma), with 2 patients undergoing a more extensive central neck or modified radical neck dissection. The remaining 20 patients had a variety of various benign disorders. There been no adverse reactions, adverse outcomes or complications associated with blood draws to measure PTH levels.

There were 3 patients (11%) that developed hypocalcemia during the immediate postoperative period. Two of the patients developed symptomatic hypocalcemia with symptoms varying from peri-oral numbness to distal extremity tingling. All 3 patients were treated with IV calcium gluconate and started on oral calcium supplementation. These hypocalcemic patients all exhibited a downward trend in serum calcium levels in the first 24 hours postoperatively, as opposed to the normocalcemic group that exhibited stable or upward trending serum calcium levels during the same period. All three patients with hypocalcemia had a greater than 80% decrease in their postoperative turbo PTH levels. In the normocalcemic group, all patients except one had a <80% decrease in their turbo PTH levels (Figure #2). The

greater than 80% drop in turbo PTH levels from preoperative to postoperative levels revealed a sensitivity of 100% and a specificity of 95.8%. The positive predictive value of turbo PTH was 75% and the negative predictive value as 100%.

Utilizing a decrement of PTH levels 80% or more as an indicator of postoperative hypocalcemia, all patients in our study would have been diagnosed intra-operatively or immediately postoperatively. The PTH assay in this study revealed a negative predictive value of 100%, meaning that the majority of our patients from this study would have been discharged soon after surgery, rather than 1-3 days later (average 2 day hospital stay in our institution). It also means that all patients that required calcium supplementation postoperatively could have been started on their supplementation up to 24 hours sooner.

These results have been corroborated with those recently published by other researchers. A retrospective study by Lindholm, et al., found PTH rapid assay as accurate as serum calcium levels as determining postoperative hypocalcemia after bilateral thyroid surgery (Surgery, 2002: 131(5): 515-520). This group utilized an absolute PTH level as the cutoff for those at risk for postoperative hypocalcemia. Another group examined PTH levels in both thyroid and parathyroid surgery and found that a 60% or greater decrement in PTH levels post-resection were indicative of postoperative hypocalcemia (Warren et al., Laryngoscope 2002: 112: 1866-1870). Most recently, Lo, et al., published results of a prospective study that utilized a 75% threshold as indicative of probable postoperative hypocalcemia with sensitivity and specificity of 100% and 72%, respectively (Annals of Surgery, 2002: 236(5): 564-9).

#### CONCLUSIONS:

Our study thus far has supported the decrement of 80% or greater as indicative of postoperative hypoparathyroidism and thus hypocalcemia. The exact percentages vary between published studies, but all point to the utility of the rapid PTH assay in total thyroidectomy patients. The utilization of this technology may enable the rapid diagnosis of postoperative hypocalcemia, and thus rapid treatment for those that require it. It will also enable the more efficient disposition of patients who are and will remain normocalcemic. It is clear that a larger population must be studied prior to any definitive altering of patient management can occur. Continued accrument of patients will strengthen our preliminary findings. More data is also needed to assess ionized calcium levels versus serum calcium levels and intact versus rapid PTH levels.

#### LIST OF PUBLICATIONS:

There are no publications/presentations/abstracts to date.

## DETAIL SUMMARY SHEET

TITLE: Not available.

KEYWORDS:

PRINCIPAL INVESTIGATOR: Winslow, Catherine P. MAJ MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Otolaryngology – Head & Neck

STATUS: W  
INITIAL APPROVAL DATE: None

### STUDY OBJECTIVE

Study withdrawn by P.I.

### TECHNICAL APPROACH

Study withdrawn by P.I.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn by P.I.

### CONCLUSIONS

Study withdrawn by P.I.

## DETAIL SUMMARY SHEET

TITLE: Not available.

KEYWORDS:

PRINCIPAL INVESTIGATOR: Winslow, Catherine P. MAJ MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Otolaryngology – Head & Neck

STATUS: W  
INITIAL APPROVAL DATE: None

### STUDY OBJECTIVE

Study withdrawn by P.I.

### TECHNICAL APPROACH

Study withdrawn by P.I.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn by P.I.

### CONCLUSIONS

Study withdrawn by P.I.



## DETAIL SUMMARY SHEET

**TITLE:** Comparing the Rate of Return of the Wheal and Flare Responses in Skin Prick Testing to Both Histamine Control and Aeroallergens After Discontinuing Two Weeks of Therapeutic Daily Dose Fexofenadine

**KEYWORDS:** Wheal and Flare Responses, Fexofenadine

**PRINCIPAL INVESTIGATOR:** Katial, Rohit, MAJ MC  
**ASSOCIATES:**

**DEPARTMENT:** Allergy-Immunology  
**SERVICE:**

**STATUS:** C  
**APPROVAL DATE:** 26 February 2002

### STUDY OBJECTIVE

The objective was to determine how long a two-week course of Allegra allergy medicine would delay the return of the wheal and flare response in patients who had a positive reaction to skin prick testing.

### TECHNICAL APPROACH

One hundred eighty volunteers from the WRAMC Allergy/Immunology Clinic with positive test results were going to be enrolled in this study. All volunteers were going to be skin prick tested to histamine, Oak, Timothy, Ragweed and dust-mite using the Greer-Pick equipment. This study design was randomized, double-blinded and placebo-controlled. The rate of return of the wheal and flare (redness and welt) was going to be measured after completing a 14-day supply of Allegra.

### PRIOR AND CURRENT PROGRESS

This study is closed. The principal and associate investigators relocated to another location.

### CONCLUSIONS

None.

## DETAIL SUMMARY SHEET

TITLE: B Cell Signaling in Human Systemic Lupus Erythematosus (SLE)

KEYWORDS:

PRINCIPAL INVESTIGATOR: Mitchell, Jeanne MAJ MC

ASSOCIATES:

DEPARTMENT: Medicine

SERVICE: Rheumatology

STATUS: W

INITIAL APPROVAL DATE: 11 June 2002

### STUDY OBJECTIVE

Study withdrawn by principal investigator prior to the protocol receiving its approval letter.

### TECHNICAL APPROACH

Study withdrawn by principal investigator prior to the protocol receiving its approval letter.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn by principal investigator prior to the protocol receiving its approval letter.

### CONCLUSIONS

Study withdrawn by principal investigator prior to the protocol receiving its approval letter.

## DETAIL SUMMARY SHEET

TITLE: GOG 0174 – A Randomized Phase III Trial of Weekly Parenteral Methotrexate vs. “Pulsed” Dactinomycin as Primary Management for Low Risk Gestational Trophoblastic Neoplasia

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott, LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecology Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 23 October 2001

### STUDY OBJECTIVE

To determine whether weekly parenteral methotrexate or “pulsed” dactinomycin is the more effective treatment for low risk gestational trophoblastic neoplasia.

To prospectively determine and compare the toxicity of each regimen.

To prospectively determine whether the definition of persistent GTN is accurate.

### TECHNICAL APPROACH

Patients with untreated, histologically confirmed low risk GTN (persistent hydatidiform mole or choriocarcinoma) will be eligible for this protocol. The patients must have a GOG Performance Status of 0, 1, or 2.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This is the first APR for this study here at WRAMC. There have been no publications reporting data from studies with similar study design in literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 40, if multi-site study. Grade IV toxicities include one other hematologic. No toxicities have been reported at WRAMC.

Ref: July 02 GOG Statistical Report

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: GOG 0194 - A Phase III Study of Adjuvant Postoperative Irradiation with or without Cisplatin/Taxol Chemotherapy Following TAH/BSO for Patients with Endometrial Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE:

STATUS: W  
INITIAL APPROVAL DATE: 20 November 2001

### STUDY OBJECTIVE

To test whether the addition of chemotherapy to radiation improves the relapse-free survival for endometrial cancer patients. To determine patterns of recurrence associated with each treatment arm. To determine the acute and late toxicity profiles associated with each treatment arm.

### TECHNICAL APPROACH

Patients with a high risk of developing endometrial cancer again after being surgically removed will be randomized to receive chemotherapy and radiation to determine if the combination will prevent the recurrence of the tumor better than radiation given alone.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This is the first APR for this study at our institute. There have been no publications reporting data from this study.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 24, if multi-site study.

### CONCLUSIONS

This study has not received final approval.

## DETAIL SUMMARY SHEET

TITLE: GOG 176 – A Phase II Trial For Pulse Actinomycin-D as Salvage Therapy For Failed Low Risk Gestational Trophoblastic Neoplasia

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecology Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 29 January 2002

### STUDY OBJECTIVE

To determine the efficacy of this actinomycin-D regimen in failed low risk Gestational Trophoblastic Neoplasia (GTN) patients.

To determine the toxicity of this actinomycin-D regimen in failed low risk GTN patients.

### TECHNICAL APPROACH

Patients who have gestational trophoblastic disease and the tumor has recurred or failed to respond to methotrexate chemotherapy will receive salvage therapy with actinomycin-D.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 31, if multi-site study. Grade 4 toxicities include 1 ANC. (Ref: GOG Statistical Report July 2002.)

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

TITLE: GOG 0185 – Phase III Randomized Study of Adjuvant Radiation Treatment Vs. Radiation and Chemotherapy in Patients With Vulvar Cancer and Involved Nodes

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecology Oncology

STATUS: C  
INITIAL APPROVAL DATE: 29 January 2002

### STUDY OBJECTIVE

To assess whether the addition of concurrent chemotherapy to inguino-femoral and pelvic nodal irradiation improves recurrence-free interval and survival in patients with carcinoma of the vulva with positive inguino/femoral lymph nodes.

To assess the toxicity of concurrent chemotherapy and inguino/femoral and pelvic nodal irradiation in patients with carcinoma of the vulva with positive inguino/femoral lymph nodes.

### TECHNICAL APPROACH

Patients with primary histologically confirmed squamous cell carcinoma of the vulva (stages I, II, and III) who are amenable to curative treatment with surgery, radiation, or both, will be randomized to receive adjuvant radiation (standard of care) or concurrent cisplatin chemotherapy to inguino/femoral lymph nodes.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 17, if multi-site study. Grade 4 toxicities have not been reported. Study was closed to patient entry 12 August 2002 due to inadequate accrual.

### CONCLUSIONS

None. Study was closed due to inadequate accrual.

## DETAIL SUMMARY SHEET

TITLE: GOG 9910 – Vaccine Therapy With Tumor Specific p53 Peptides in Adult Patients With Low Burden Adenocarcinoma of the Ovary

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics & Gynecology  
SERVICE: Gynecology Oncology Group

STATUS: O  
INITIAL APPROVAL DATE: 12 February 2002

### STUDY OBJECTIVE

### TECHNICAL APPROACH

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Approval letter is dated 23 April 2003, therefore no FY03 APR is due in February 2003.

### CONCLUSIONS

Approval letter is dated 23 April 2003, therefore no FY03 APR is due in February 2003.

## DETAIL SUMMARY SHEET

TITLE: GOG 0146M - A Phase II Evaluation of Tirapazamine (NSC#130181, IND 45,525) in Combination With Cisplatin in the Treatment of Recurrent Platinum Sensitive Ovarian or Primary Peritoneal Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: GOG

STATUS: O  
INITIAL APPROVAL DATE: 28 May 2002

STUDY OBJECTIVE:

To estimate the antitumor activity of Tirapazamine and platinum in patients with persistent or recurrent platinum-sensitive ovarian or primary peritoneal cancer. To determine the nature and degree of toxicity of Tirapazamine and platinum in this cohort of patients.

TECHNICAL APPROACH

After the initial screening the patient will receive the drug Tirapazamine and cisplatin every 3 weeks. The Tirapazamine will be infused into the vein over 2 hours, followed 1 hour later by cisplatin, which will be infused into the vein over 30 minutes. The minimum treatment period is one course (3 weeks of actual treatment), however 6 courses is the standard measuring period for GOG. Each course will be repeated every 3 weeks, depending on the patient recovery from side effects. Thus prior to each treatment, a history including a physical examination, blood test, and urinalysis will be performed. In addition, if the baseline measurements for the CA-125 and audiogram results are not within normal range, these tests will be repeated as well. The patient will give approximately 19 tablespoons of blood for the blood test and drug levels will not be tested. If the patient responds to treatment and the side effects are not severe, the patient may remain on the study indefinitely at the investigators' discretion. After completion of treatment, the patient will receive follow up appointments every 3 months for the first 2 years, then every 6 months for the next 3 years and annually thereafter. These follow up appointments may include a physical exam, blood tests, and chest x-rays. All or part of the patient's medical records will be sent to the GOG Administrative Office in Philadelphia, PA, as well as to the GOG Statistical Office in Buffalo, NY, to be reviewed and analyzed by doctors and other study personnel, along with the records of all other patients participating in this study from this and other institutions.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no publications reporting data from this study or from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 40, if multi-site study. No Grade 4 toxicities were reported. This study was suspended on 4 March 2003 pending initiation of second phase accrual.

CONCLUSIONS:

Too early.



## DETAIL SUMMARY SHEET

TITLE: GOG 0170-C – A Phase II Trial of ZD1839 (IRESSA <sup>TM</sup>) (NSC #715055, IND #61187) in the Treatment of Persistent or Recurrent Epithelial Ovarian or Primary Peritoneal Carcinoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rose, G. Scott LTC MC

ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology

STATUS: O

SERVICE: Gynecology Oncology Group

INITIAL APPROVAL DATE: 30 July 2002

### STUDY OBJECTIVE

- a. To determine the level of epidermal growth factor receptor (EGFR) expression and that of activated EGFR (pY-EGFR) in archived formalin-fixed and paraffin embedded primary tumor sample collected prior to the initiation of first-line therapy.
- b. To determine the level of EGFR and pY-EGFR from formalin-fixed and paraffin embedded core biopsy from a metastatic site collected within 14 days before starting ZD1839 and then again upon completion of 8 weeks of ZD1839 therapy (2x28 day cycle).
- c. To assess whether exposure to ZD1839 tends to decrease the level of activated EGFR and EGFR kinase activity.

### TECHNICAL APPROACH

Phase II open label trial evaluating efficacy and safety of ZD 1839 in approximately 56 patients following initial platinum/paclitaxel-based chemotherapy. Medications will be given as 500mg orally as a daily dose continuously until disease progression or toxicity warrants removal from treatment. Clinical labs will be measure monthly. Radiographic studies for monitoring purposes will be conducted every 60 days.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

None. Too early.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 30, if multi-site study.

### CONCLUSIONS

None. Too early.

## DETAIL SUMMARY SHEET

TITLE: The Chemoprotective Effects of Progestin On The Endometrial Lining

KEYWORDS:

PRINCIPAL INVESTIGATOR: Maxwell, G. Larry MAJ MC

ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology

STATUS: O

SERVICE: Gynecologic Oncology Group

INITIAL APPROVAL DATE: 29 November 2001

### STUDY OBJECTIVE

To test the hypothesis that progestins provide a chemoprotective effect against endometrial cancer through induction of apoptosis, PTEN, and TGF-beta in the endometrium. To identify the other chemoprotective changes in genomic expression within the endometrium that occur secondary to progestin use. This research will not focus on identification of hereditary genetic alterations.

### TECHNICAL APPROACH

All patients undergoing assessment for surgery for benign gynecologic conditions that do not involve irregular menstrual bleeding will be approached regarding participation in this trial. The patients will receive progestin levonorgestrel or a placebo pill on a daily basis for four weeks prior to undergoing surgery.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since this protocol's review one year ago, there have been no publications reporting data from studies with similar study design in the literature.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

Too early.

## DETAIL SUMMARY SHEET

**TITLE:** RF BION® - An Injectable Microstimulator For The Treatment of Refractory Urinary Urge Incontinence in Women

**KEYWORDS:** Neuromodulation, neurostimulator, microstimulator, pudendal nerve, pudendal nerve stimulation, urinary urge incontinence, percutaneous stimulation test

**PRINCIPAL INVESTIGATOR:** Buller, Jerome L., MAJ MC

**ASSOCIATES:** Ernest Lockrow, LTC MC, G. Scott Rose, LTC MC, James R. Jezior, LTC MC, Kathleen A. Noel, RN MS

**DEPARTMENT:** Obstetrics and Gynecology  
**SERVICE:**

**STATUS:** O  
**INITIAL APPROVAL DATE:** 29 January 2002

### STUDY OBJECTIVE

Research hypothesis: Chronic electrical stimulation of the pudendal nerve via the RF BION® microstimulator is a feasible treatment for refractory urge urinary incontinence in women.

Goals of the study:

1. To determine the feasibility of the RF BION® microstimulator is a feasible treatment for refractory urge urinary incontinence in women.
2. To evaluate the response of the lower genitourinary tract to chronic electrical stimulation of the pudendal nerve by the RF BION® as measured by cystometrogram and voiding diary parameters.
3. To determine sensory and pain thresholds of electrical stimulation based on patients' perception.
4. To evaluate patient acceptance of chronic electrical stimulation of the pudendal nerve via the RF BION®.
5. To monitor for adverse events with implantation and use of the RF BION®.

### TECHNICAL APPROACH

Methodology: Anti-incontinence medication or the use of other stimulation equipment for urge incontinence will be discontinued seven days before the preliminary testing. With the patient in the dorsal lithotomy position the urodynamic catheters are placed through the urethra into the bladder and into the rectum. A standard CMG will then be performed. For the PST, a local anesthetic, 102 cc of a 1% lidocaine without epinephrine, will be injected into the skin at the insertion site approximately 1.5cm medial to the ischial tuberosity on the lateral perineum. (The insertion site for the PST and the implant are the same.) Percutaneous electrical stimulation of the pudendal nerve will then be performed utilizing a transperineal approach. This involves inserting a stimulating electrode through the skin of the perineum, through the ischial rectus fossa, to the pudendal nerve located in Alcock's canal adjacent to the ischial spine. Proper electrode placement will be confirmed by monitoring the stimulated response at external urethral sphincter and external anal sphincter recordings, perineal nerve terminal motor latency (PeNTML) and pudendal nerve terminal motor latency (PNTML), respectively. Sensory and pain thresholds for electrical stimulation will be obtained by gradually increasing the stimulation amplitude and requesting that the patient identify the level at which sensation is first identifiable and the point at which sensation becomes painful. Stimulation parameters such as amplitude, pulse duration, and frequency will be modified in an effort to maximize the stimulus in terms of appropriate electrodiagnostics responses, urodynamic parameters, and patient comfort. After the screening PST, the patient may resume any medication or the use of other stimulation equipment for urge urinary incontinence unless implantation of the RF BION® is planned within seven days.

A positive PST is represented by a 50% increase in maximum cystometric capacity (MCC) during percutaneous stimulation as compared to the baseline MCC obtained without stimulation. The maximum cystometric capacity is the bladder volume at which the patient can no longer delay voiding. Pretreatment evaluation includes a medical history, completed urogynecologic questionnaire, three-day voiding diary, baseline pain scale and quality of life

index, PST, and CMG. Post activation evaluation includes a CMG and a three-day voiding diary and pain scale index. Post treatment evaluation at 194 days includes a CMG, three-day voiding diary, pain scale, and general and disease specific quality of life measures. Pain will be assessed using a visual analog scale. The Incontinence Impact Questionnaire (IIQ) and the Urinary Distress Inventory (UDI) assesses the impact of urinary incontinence on activities of daily living and the degree of bother caused by the incontinence, respectively. Data on the reliability, validity, and sensitivity to change of these measures demonstrate that they are psychometrically strong. General health related quality of life will be assessed using the SF 36. The IIQ, UDI, and SF36 will be administered twice – once at the screening visit and once at the day 194 post-treatment visit.

No modifications will be undertaken in the RF BION® methodology in the future.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No amendments or modifications to the research study have occurred since protocol approval in May of 2002.

Activity in this study was temporarily stopped due to the expiration of the original CRDA in April 2002. The original CRDA was based on our projected start and finish times. However, the protocol was approved one month after the expiration of the original CRDA. Once we identified this problem, all research activity on this protocol was suspended while awaiting the amended CRDA. A new CRDA was signed between Advanced Bionics Corporation and T.R.U.E. Research Foundation with amendment approval issued in September of 2002.

Enrollment in the RF BION® continues to be ongoing and has not yielded as many participants as initially anticipated. Chart reviews were undertaken in Women's Health from 1999 to the present to identify potential participants. One participant received preliminary testing and was not able to qualify as a candidate due to the results obtained from CMG testing. Recruitment has been difficult due to two reasons. First, this prototype microstimulator uses bulky external devices, which are worn and maintained as part of the study, and were found potentially imposing to many participants. Additionally, the final bion®, which is entirely self-contained, and does not involve the bulky external devices, is currently available. During the informed consent process, potential study participants were informed of the status of the new device. Many potential participants are electing to wait for the final device to become available. We are preparing a protocol utilizing this new device for clinical trials here at WRAMC.

No adverse reactions have occurred to date with this study.

The number of subjects enrolled to the study since last APR at WRAMC is 1 and the total enrolled to date at WRAMC is 1.

#### CONCLUSIONS

With the current status of this study, no findings have been obtained to date.

## DETAIL SUMMARY SHEET

**TITLE:** RF BION® - An Injectable Microstimulator For The Treatment of Refractory Urinary Urge Incontinence in Women

**KEYWORDS:** Neuromodulation, neurostimulator, microstimulator, pudendal nerve, pudendal nerve stimulation, urinary urge incontinence, percutaneous stimulation test

**PRINCIPAL INVESTIGATOR:** Buller, Jerome L., MAJ MC

**ASSOCIATES:** Ernest Lockrow, LTC MC, G. Scott Rose, LTC MC, James R. Jezior, LTC MC, Kathleen A. Noel, RN MS

**DEPARTMENT:** Obstetrics and Gynecology  
**SERVICE:**

**STATUS:** C  
**INITIAL APPROVAL DATE:** 29 January 2002

### STUDY OBJECTIVE

Research hypothesis: Chronic electrical stimulation of the pudendal nerve via the RF BION® microstimulator is a feasible treatment for refractory urge urinary incontinence in women.

Goals of the study:

1. To determine the feasibility of the RF BION® microstimulator is a feasible treatment for refractory urge urinary incontinence in women.
2. To evaluate the response of the lower genitourinary tract to chronic electrical stimulation of the pudendal nerve by the RF BION® as measured by cystometrogram and voiding diary parameters.
3. To determine sensory and pain thresholds of electrical stimulation based on patients' perception.
4. To evaluate patient acceptance of chronic electrical stimulation of the pudendal nerve via the RF BION®.
5. To monitor for adverse events with implantation and use of the RF BION®.

### TECHNICAL APPROACH

Methodology: Anti-incontinence medication or the use of other stimulation equipment for urge incontinence will be discontinued seven days before the preliminary testing. With the patient in the dorsal lithotomy position the urodynamic catheters are placed through the urethra into the bladder and into the rectum. A standard CMG will then be performed. For the PST, a local anesthetic, 102 cc of a 1% lidocaine without epinephrine, will be injected into the skin at the insertion site approximately 1.5cm medial to the ischial tuberosity on the lateral perineum. (The insertion site for the PST and the implant are the same.) Percutaneous electrical stimulation of the pudendal nerve will then be performed utilizing a transperineal approach. This involves inserting a stimulating electrode through the skin of the perineum, through the ischial rectus fossa, to the pudendal nerve located in Alcock's canal adjacent to the ischial spine. Proper electrode placement will be confirmed by monitoring the stimulated response at external urethral sphincter and external anal sphincter recordings, perineal nerve terminal motor latency (PeNTML) and pudendal nerve terminal motor latency (PNTML), respectively. Sensory and pain thresholds for electrical stimulation will be obtained by gradually increasing the stimulation amplitude and requesting that the patient identify the level at which sensation is first identifiable and the point at which sensation becomes painful. Stimulation parameters such as amplitude, pulse duration, and frequency will be modified in an effort to maximize the stimulus in terms of appropriate electrodiagnostics responses, urodynamic parameters, and patient comfort. After the screening PST, the patient may resume any medication or the use of other stimulation equipment for urge urinary incontinence unless implantation of the RF BION® is planned within seven days.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

### CONCLUSIONS

Study was terminated due to the accelerated development of the next generation microstimulator.

## DETAIL SUMMARY SHEET

TITLE: Early Detection of Gynecologic Cancer Using Proteomics Based SELDI-TOF Method and a Heuristic Algorithm of Data Analysis

PRINCIPAL INVESTIGATOR: Maxwell, G. Larry, MAJ, MC

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Division of GYN Oncology

STATUS: O  
INITIAL APPROVAL DATE: 28 May 2002

STUDY OBJECTIVE:

To determine the accuracy of the proteomics based SELDI-TOF test in the early detection of gynecologic cancer.

TECHNICAL APPROACH

*Collection:* A query of the Army Medical Surveillance Activity identified patients with a diagnosis of malignancy who had serum collected at least two months (or longer) from their diagnosis of cancer. In order to confirm the diagnosis of cancer in these patients, the Army Medical Surveillance Activity will provide a list of the patients as well as where their diagnosis of cancer was made. The confirmation of diagnosis is essential in order to obtain accurate information for validation of this new technology. Patients admitted to the hospital may have a presumptive diagnosis of ovarian cancer based on a suspicious pelvic mass. In many instances, the patient leaves the hospital postoperatively before the final diagnosis returns. Unfortunately, the medical record in most instances will not be amended to reflect the final diagnosis. Two situations could potentially occur: A benign appearing mass turns out to be a cancer or a cancerous appearing mass turns out to be benign. For the purposes of training the artificial intelligence, it is essential to determine the correct diagnosis. Dr. Chris Zahn is a gynecologic pathologist at the Uniformed Services University of the Health Sciences (USUHS) who also serves as the OB/GYN consultant to the Air Force Surgeon General and will not be involved with the proteomics analysis of serum samples. Dr. Zahn has agreed to review the slides from patients on the list provided by AMSA. Dr. Zahn will request the slides. Dr. Zahn will review them at USUHS. The requested slides or tissue used to prepare a slide will be used to confirm the original diagnosis only. There will be no request for tissue to be used for research purposes. The requested slides or tissue used to prepare a slide will be used to confirm the original diagnosis. Only those patients who are confirmed with malignancy will be included in this study. Pathologic information gained from examination of the slides will be submitted along with the list of patients confirmed with cancer back to the Army Medical Surveillance Activity who will coordinate with the DoD Serum Repository in providing serum samples and the clinical data in a de-identified and un-linked format to the investigators. The investigators will not be able to make a link between serum samples, clinical data, and patient identity. Controls will be matched to cancer cases in terms of the time that the serum sample was collected (+/- 30 days), age (+/- 1yr), race, gender and Body Mass Index (BMI +/- 0.1) at the time of entry into the military. In instances in which there is no height and/or weight recorded for the cancer cases, the matching criteria will be relaxed for these variables and the case will be matched for the other variables (time of collection, age, race, gender). Sample volumes (300 µL) will be requested. The SELDI analysis can be done on as little as 10 µL of sample per run and volumes for replicates are needed. In addition, random samples will be subjected to quality assurance and quality control measures including repetitive sampling between and within days on at the NCI/FDA. The total consumption is anticipated not to exceed 300 µL of serum.

*\*Sample analysis:* SELDI analysis will be performed using an aliphatic reverse phase chip (Ciphergen, Palo Alto, CA), with bait surfaces that have been pretreated with acetonitrile. Ten µL of serum will be applied directly to the bait surface of the chip prior to addition of the energy-absorbing molecule (sinapinic acid) that will be allowed to crystallize.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE: There has been no recent literature relating to the subject of this study. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. No grade 4 toxicities have been reported.

CONCLUSIONS: Too early. This study, although originally approved in May 2002, has had pending amendments that have only been recently approved. This study will begin next month (May 2003).

## DETAIL SUMMARY SHEET

TITLE: IM-D-CEA-C14 Pharmacokinetics and Biodistribution of Multiple Administrations of CEA-Scan (Arcitumomab) Following Complete Resection of Primary Colorectal Carcinoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Bridwell, Robert S. MAJ MC  
ASSOCIATES:

DEPARTMENT: Radiology  
SERVICE: Nuclear Medicine

STATUS: O  
INITIAL APPROVAL DATE: 15 January 2002

### STUDY OBJECTIVE

### TECHNICAL APPROACH

No modifications.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. No patients enrolled to date – the approval date was in early November of 2002.

### CONCLUSIONS

None.

## DETAIL SUMMARY SHEET

TITLE: What is The Sensitivity of Tc-99m Apcitide to Detect Pulmonary Emboli?

KEYWORDS:

PRINCIPAL INVESTIGATOR: MAJ Robert S. Bridwell MC  
ASSOCIATES:

DEPARTMENT: Radiology  
SERVICE: Nuclear Medicine

STATUS: O  
INITIAL APPROVAL DATE: 9 April 2002

### STUDY OBJECTIVE

To define the sensitivity of Technetium 99m-apcitide (Tc99m-apcitide) to detect acute pulmonary emboli.

### TECHNICAL APPROACH

Prospective trial evaluating the sensitivity of Tc-99m depreotide in patients who present with an acute pulmonary embolus.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No patients have been enrolled to date. No new data exist to support a change in the protocol.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

Ongoing study that has just started with no patients enrolled to date.



## DETAIL SUMMARY SHEET

TITLE: IM-D-MN3-22 Phase II Study of LeukoScan Imaging in Patients With Acute Anthrax Infections

KEYWORDS:

PRINCIPAL INVESTIGATOR: Bridwell, Robert S. MAJ MC

ASSOCIATES:

DEPARTMENT: Radiology

SERVICE: Nuclear Medicine

STATUS: O

INITIAL APPROVAL DATE: 14 May 2002

### STUDY OBJECTIVE

Imaging patients with acute anthrax to assess the sensitivity of LeukoScan.

### TECHNICAL APPROACH

Prospective trial in patients' diagnosis with anthrax to document the sensitivity of LeukoScan and to reassess their response to therapy based on an imaging basis.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study. No new data because there have been no cases reported since the start of the protocol.

### CONCLUSIONS

None can be drawn.

## DETAIL SUMMARY SHEET

**TITLE:** An Open Label, Multicenter, Clinical Study to Evaluate the Diagnostic Utility of LeuTech® Scintigraphy for the Detection of Inhalational Anthrax in Patients Who Have Symptoms of or Consistent With a Diagnosis of Inhalational Anthrax

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** Bridwell, Robert S., MAJ MC  
**ASSOCIATES:**

**DEPARTMENT:** Radiology  
**SERVICE:** Nuclear Medicine

**STATUS:** O  
**INITIAL APPROVAL DATE:** 16 July 2002

### STUDY OBJECTIVE

This study will evaluate the diagnostic utility of technetium Tc99m anti-CD IgM (Tc99m LeuTech®) Scintigraphy for the detection of inhalational anthrax in patients who have symptoms suggestive of or consistent with a diagnosis of inhalational anthrax, but without a confirmed diagnosis.

### TECHNICAL APPROACH

This is an open-label within-patient, comparative clinical study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No literature. No patients have been enrolled.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

### CONCLUSIONS

No patients enrolled. No conclusions can be drawn.

## DETAIL SUMMARY SHEET

TITLE: A Pilot Open Label Clinical Study to Evaluate Pulmonary Imaging with LeuTech®.

KEYWORDS:

PRINCIPAL INVESTIGATOR: Bridwell, Robert S., MAJ MC  
ASSOCIATES:

DEPARTMENT: Radiology  
SERVICE: Nuclear Medicine

STATUS: O  
INITIAL APPROVAL DATE: 16 July 2002

### STUDY OBJECTIVE

1. Evaluate the performance of LeuTech® in the context of common pulmonary pathologies that may co-present with pulmonary anthrax.
2. Refine the current pulmonary imaging parameters.
3. Develop image interpretation guidelines for ongoing and future clinical studies.

### TECHNICAL APPROACH

The study is a pilot, open-label, clinical study to evaluate pulmonary imaging with LeuTech®.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

### CONCLUSIONS

None can be drawn. No patients enrolled.

## DETAIL SUMMARY SHEET

TITLE: Multi-Center Trial of Detection of Colorectal Neoplasm by CT Virtual Colonoscopy in a Screening Population

KEYWORDS:

PRINCIPAL INVESTIGATOR: Choi, Jong-Ho R. MAJ MC

ASSOCIATES: Pickardt, Perry J. LCDR MC, USN; Feuerstein, Irwin, MD; Hwang, Inku MAJ MC; Brazaitis, Michael COL MC; Wong Roy COL, MC

DEPARTMENT: Radiology

STATUS: O

SERVICE: Diagnostic Radiology

INITIAL APPROVAL DATE: 29 January 2002

### STUDY OBJECTIVE

The specific aim of our research study is to assess the diagnostic performance of computed tomography (CT) virtual colonoscopy (VC) for the detection of colorectal neoplasm in a screening population. This technology has shown early promise for noninvasive detection of colonic polyps and cancers in high-risk patients. Colorectal cancer is a common malignancy that is largely preventable by effective screening. However, only a fraction of the recommended patient population is currently being screened. Standard optical colonoscopy (OC) is an effective screening tool but is moderately invasive and relatively expensive. A cost-effective screening examination of the entire colon that is less invasive and more acceptable to patients could potentially increase the number of patients studied and therefore improve overall survival. However, before advocating CT VC for screening in the general population, its diagnostic performance in this setting must be demonstrated against a proven method.

### TECHNICAL APPROACH

Total colonic examination is performed by CT VC following a modified colon preparation with subsequent OC performed on the same day to serve as the reference for comparison. The study methodology has not been changed from its final approved protocol.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The overall sensitivity and specificity of virtual colonoscopy for patients (130 patients completed at WRAMC) with polyps 10 mm and greater is 85.7% (6/7) and 97.6% (120/123), respectively. The call back rate (percentage of patients that would need to be called back for optical colonoscopy in a theoretical VC only screening scenario) is 6.9% (9/130) with a 66.7% (6/9) positive call back rate (percentage of called back patients with true colonic polyps on optical colonoscopy). The negative predictive value of the screening study is 99.2% (120/121). No serious adverse events have occurred locally or at other sites to this date.

The number of subjects enrolled to the study since last APR at WRAMC is 213 and the total enrolled to date at WRAMC is 213. The total number enrolled study-wide is 625, if multi-site study.

### CONCLUSIONS

The study demonstrates that VC is both sensitive and specific for the detection of colonic polyps, 10mm and greater, in a screening population. Furthermore, the early results suggest that VC can reliably differentiate between those patients that will require additional work-up with optical colonoscopy and those patients that can be followed with imaging study alone. If the statistical data continues to hold with additional patients, this will validate VC as a reliable screening modality for evaluation of significant colonic polyps. Additional work is needed to increase the statistical validity of the current study, as the prevalence of significant polyps in the studied screening population is still very low (7/130).

## DETAIL SUMMARY SHEET

**TITLE:** Detection of Glenoid Labral Tears and Rotator Cuff Tears – Comparison of Intravenous Contrast-Enhanced and High-Resolution Non-Contrast MR Imaging of the Shoulder

**KEYWORDS:** Shoulder, MR; Shoulder, injuries; Gadolinium

**PRINCIPAL INVESTIGATOR:** Dinauer, Philip A. MAJ MC

**ASSOCIATES:** William Doukas, M.D., LTC, MC; Kevin Murphy, M.D., LTC, MC; Tom Hash, LCDR, M.D.; Ron Lehman, M.D., CPT, MC; Richard Islinger, M.D., MAJ; and Neil Gambill, M.D.

**DEPARTMENT:** Radiology

**STATUS:** O

**SERVICE:** Diagnostic Radiology

**INITIAL APPROVAL DATE:** 14 May 2002

### STUDY OBJECTIVE

The primary objective of this research is to prospectively compare the accuracy of noncontrast and gadolinium contrast-enhanced magnetic resonance imaging (MRI) in defining glenoid labral-ligamentous and rotator cuff tears of the shoulder. Our hypothesis is that the contrast-enhanced studies will be more accurate than the noncontrast high-resolution images in defining soft tissue injuries of the shoulder and that the contrast-enhanced studies will compare favorably with published accuracy results for an alternate gadolinium-enhanced technique, MR arthrography. A sub objective of this research is to compare axial fat-suppressed fast spin echo (FSE) proton density weighted and post-gadolinium fat-suppressed T1-weighted images in the evaluation of anterior and posterior labral tears by an inexperienced observer (a radiology resident), a body imager, and two experienced musculoskeletal radiologists.

### TECHNICAL APPROACH

**Study Design:** This is a prospective, interventional study in which patients undergo research with a high-resolution noncontrast as well as a gadolinium-enhanced shoulder MRI prior to receiving surgery (arthroscopic and/or open shoulder surgery) as the standard of care for their shoulder disorder. The radiologists study the MR images for presence or absence of rotator cuff tear and glenoid labral tear. The presence or absences of rotator cuff or labral tear are determined by the gold standard, surgical inspection.

**Methodology:** Researchers from the Department of Orthopedics and Rehabilitation at WRAMC identify patients in the orthopedic or sports medicine clinics who qualify for shoulder surgery as the standard of care to define and treat either a suspected rotator cuff or capsulolabral injury. The orthopedic surgeons offer patients a research MRI prior to their operation. For those patients who express an initial interest in obtaining a research MRI, the surgeon completes a Reason for Surgery form that the patient takes to the nurse case manager in the orthopedic department. The surgery is scheduled. Dr. Dinauer obtains consent, generates a patient research chart, and schedules the patient for a 90 minute MRI research slot (see Table 1). When at the Pentagon or at Carlisle Barracks, the nurse collects the Reason for Surgery form and submits this document to Dr. Dinauer upon returning to WRAMC. Dr. Dinauer calls these patients to obtain initial verbal consent, arranges the date of MRI, and then obtains written consent. Patients also complete a pre-operative Research Questionnaire. If a patient prefers to take time to consider the protocol, the MR will not be scheduled. Dr. Hash or Dr. Dinauer will call the patient within ten days for a final decision. Those patients who wish to participate will then be given an MR appointment and these patients will provide consent and complete their questionnaires prior to the MRI on the day of the test. All MR examinations will be performed using either of the two 1.5 Tesla GE MRI systems within the radiology department at WRAMC. All MR appointments must be made within three months of the planned date of surgery.

Table 1: Sequence of Events in Shoulder Research Protocol

1 week or month before	Research Test	One week later	1 month later	2 months later	3 months later
1. Recruit 2. Reason for surgery 3. Informed consent discussion 4. Questionnaire 5. Schedule MRI	-Perform MRI without and with gadolinium contrast	-Rater A first interprets MRI without contrast (initial 20 patients, then (+)contrast for next 20 patients, and so on...) -Rater A, C and D) interpret 256 freq. axials instead of 512 freq. axials (for first 20 patients, then reverse sequence for next 20, etc.)	-Shoulder surgery	-Rater A, C and D blindly, randomly interpret MRI with contrast (for first 20 pts) -Rater B interprets MRI with contrast (for first 20 patients)	-Rater B interprets MRI without contrast - Rater A, C and D blindly, randomly review FSE axials on first group of 20 patients

There will be four raters for all MRI exams: rater A is Dr. Dinauer. Rater B is Dr. Flemming, from National Naval Medical Center. A third rater (Rater C) is a fellowship trained body imager. The fourth rater (Rater D) is the PGY-2 radiology resident. Raters are blinded to patient history during each interpretation session. Within 7 days of the conclusion of each MR examination, rater A reviews either gadolinium-enhanced or noncontrast images on computer monitors of the AGFA picture archive and communications system (P.A.C.S.). When reviewing noncontrast studies, rater A selects only one of the axial image series for initial review. Also, raters C and D interpret only one set of axial images from the same study and list findings on an Axial Image Data Sheet. Raters will not search for or retrieve any old patient records that may provide radiographic results on studies performed prior to enrollment in the research protocol. Rater A completes a MRI Data Sheet. The surgeon will be given a copy of results via CHCS. MRI data sheets are placed in each patient's research file, which will be maintained in the principal investigator's office. Each patient will have one CHCS radiology examination number to correspond to the without and with contrast shoulder exams. Once Rater A reviews these exams, Rater A enters findings into CHCS. This will allow physicians and patients to access these official reports for inclusion in their medical records. Also, patients will be able to discuss results provided in CHCS with their surgeon prior to the operation. While randomizing the order of the MRI readings may be optimal, for ethical reasons we have determined that rater A will review one of the two sets of images (either noncontrast or contrast sets) after each study is performed to inform the surgeon of findings which could influence the decision to alter surgical approach from an arthroscopic to an open procedure (e.g., presence of a Bankart tear). Therefore, rater A will initially know patient identifiers (e.g., name, age and sex). However, the MR interpretations will be randomized to the extent that radiologist A will interpret the noncontrast examinations of the initial 20 patients prior to interpreting the sets of contrast images in the same group of 20 patients at least 4 weeks later. When rater A randomly reviews the contrast images 4 weeks later, rater A is blinded to patient identification. Raters C and D are also blinded as they interpret only axial contrast images. Rater B will interpret the MR studies in separate sessions and in a reverse order from Rater A. That is, he will interpret the initial 20 contrast examinations instead of the noncontrast examinations. Then, for the next group of patients (#21 – 40), rater A and rater B will swap order of review. This swapping of order between rater A and B will continue until the end of the study. While reviewing the research images, raters will complete an MRI Data Sheet. This sheet requires the radiologist to grade the labrum for "tear" or "no tear". Presence of a tear will be subcategorized as "definite tear", "probable tear" or "possible tear." The "no tear" category is subcategorized as "normal" or "probable normal variant/degeneration". Tears involving the superior labrum are categorized according to the Snyder classification of superior labral anterior-to-posterior tears (types 1-4). Normal variants such as sublabral foramina and anterior labral absence (Buford complex) will be described. Whenever possible, anteroinferior labral tears will be further categorized as Bankart, Perthes', or ALPSA lesions. If adequately seen, the glenohumeral ligaments will be described as normal or abnormal (with irregular, wavy shape or tear). Paralabral ganglion cysts (usually associated with labral tears) will also be described. For the rotator cuff, which is composed of four convergent tendons, the radiologist will grade each tendon for "tear" or "no-tear." The "no tear" category includes a normal tendon and tendinopathy (degeneration). Torn tendons will be further described as full-thickness or partial-thickness tears, with accompanying measurements. Location of a partial-thickness tear within the tendon will be recorded as intrasubstance (interstitial), bursal surface or articular surface. For partial tendon tears, an estimated percentage of torn tendon width will be given (< 50% or > 50%). The long biceps tendon will be characterized as normal, degenerated, torn or subluxed. Osseous findings associated with impingement or

instability will be described. There will be a section on the data sheet for describing unexpected or rare findings (e.g., a tumor).

Experienced shoulder surgeons will determine the surgical findings. The surgeons work separately and will not collaborate in describing the surgical findings for any single patient. The surgeons will inspect the articular surface and bursal surface of the rotator cuff in those patients with suspected cuff injury. Whereas the articular surface of the rotator cuff will routinely be inspected in those patients with suspected labral injury, the bursal surface of the cuff may not be inspected as an additional incision through the deltoid to the subacromial space would not always be indicated in these patients. However, in those patients with suspected labral tear that have an unsuspected bursal surface rotator cuff tear on MRI, the surgeon may choose to alter his surgical approach and arthroscopically inspect the subacromial space. The Surgical Data Sheet addresses a similar list of items as on the MRI data sheet. At the completion of the operation, the surgeon will submit a Surgical Data Sheet to Dr. Hash or Dinauer, who will collect copies of these data sheets from Dr. Lehman on a monthly basis. Surgical results for any individual patient will not be shared with any of the raters until after all MR images are reviewed or until the end of the research study.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Recent literature has not discussed research questions addressed in this protocol.

Since the initial approval of this protocol in May 2002, the Department of Clinical Investigation has approved several modifications. We have added two associate investigators: Dr. Richard Islinger as a surgical investigator and Dr. Neil Gambill as an additional MRI interpreter. Also, Dunham U.S. Army Health Clinic has been approved as an additional site of subject recruitment. A CRDA for this protocol was approved on 8 October 2002. Magnevist contrast granted from Berlex Laboratories is now being used instead of contrast purchased exclusively through the radiology department budget.

Twenty-six subjects were enrolled last year in the months of September through December, 2002. A total of 66 subjects have been enrolled to date, and 44 of these subjects have completed their shoulder surgery. All subjects are military health care beneficiaries over age 18 years. Ten of the subjects have been women. None have requested or required urine screening for suspected pregnancy.

There have been no adverse events in any of these 66 subjects. No subjects have completely withdrawn from the study, although three will likely withdraw in the next three months. These three have decided to delay surgery and continue with physical therapy.

Surgical findings in the first 18 subjects were correlated with the MRI findings in order to present preliminary results at a skeletal radiology meeting. Eleven of the 18 subjects had rotator cuff tears, and 9 of these were partial tears. The other 2 tears were full-thickness tears. Seventeen of the 18 subjects had glenoid labral injury that required either debridement or repair. For the radiology meeting, only superior labral injuries were reviewed, and a total of 14 patients had injury at the superior labrum. The MRI raters (A-D) were 61 - 83% accurate in detecting superior labral injury with use of intravenous gadolinium, and two of the four raters had improved accuracy with the contrast. For rater A and D, there was no difference in accuracy when comparing noncontrast and contrast-enhanced images.

#### CONCLUSIONS

Based on results from the first 18 patients, we conclude that the association between partial rotator cuff tear and glenoid labral injury (tearing or fraying) may be higher than initially expected. There have been no confirmed patient disenrollments to date. Therefore, we may be able to reach our goal of MRI and surgical evaluation of 50 partial cuff tears and 50 labral tears after recruiting 120 - 150 subjects, instead of 230 subjects as originally requested. Once we obtain 100 enrolled patients, we plan to tabulate the total number of cuff and labral injuries and reassess our target number of subject enrollment. Given the small sample size thus far, we are unable to conclude whether use of intravenous contrast material makes a statistically significant difference in our ability to detect partial rotator cuff tears or glenoid labral tears. Further data collection and analysis are required.

## DETAIL SUMMARY SHEET

TITLE: Ultrasound Mediated Tissue Preservation (UMTP)

KEYWORDS:

PRINCIPAL INVESTIGATOR: Andriko, JoAnn LTC MC  
ASSOCIATES:

DEPARTMENT: Pathology and Area Laboratories  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 26 February 2002

### STUDY OBJECTIVE

To attempt to develop a novel system for rapid analysis and standardization of tissue preservation and processing. The ultrasound-mediated high-speed tissue fixation and processing technique described herein provides rapid turn-around time and high quality protein and RNA/DNA preservation. The purpose is to determine the degree of antigenic (protein) and macromolecular (DNA and RNA) preservation possible during UMTP (ultrasound mediated tissue processing). Sophisticated antigenic and macromolecular testing will be performed in parallel on all tissues collected, including immunoperoxidase staining, RT-PCR, PCR, and ISH studies.

### TECHNICAL APPROACH

Gross autopsy tissue samples are being collected and processed by UMTP and by traditional FFPE methods. Tissues will be subsequently tested for the above antigenic and macromolecular preservation. By using a specially designed high frequency/high intensity ultrasound by WSC, we irradiated single tissue sample with this ultrasound device for 3-15 minutes when the tissue was step-by-step placed in 200ml of formalin, and routine overnight alcohol, xylene, and paraffin processing. To demonstrate the unique quality of US-mediated high-speed tissue fixation and processing, we equally divided each tested tissue into two fragments (thickness < 5mm). One fragment was processed with routine 10% formalin fixation (12 hours) and overnight processing. The other half was processed through UMTP as described above. The time that was required for routine tissue processing was 30 hours vs. <1 hour using USTP.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

On 9 September 2002, we received final approval by the Walter Reed Clinical Investigation Committee and the Walter Reed Human Use Committee for use of human tissues obtained from adult autopsies. In November 2002, fourteen tissue specimens were obtained from the first autopsy case. At the present time, we are assessing tissue morphology on H and E stained slides, and further evaluating the US processed tissue using standard IHC, ISH, and RT-PCR techniques.

The number of "subjects" enrolled to the study since last APR at WRAMC is 50 and the total enrolled to date at WRAMC is 50.

### CONCLUSIONS

This technology can be used for a rapid biological warfare agent diagnosis. No presentations on this current research protocol have been made. No publications have been made to date.



## DETAIL SUMMARY SHEET

TITLE: Oxidative and Nitrosative Stress in Carcinogenesis of CTCL in Archived Tissue Samples From Patients Diagnosed With Mycosis Fungoides (MF)

PRINCIPAL INVESTIGATOR: Marrogi, Aizen J., LTC MC

DEPARTMENT: Pathology and Area Laboratories  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 24 September 2002

### STUDY OBJECTIVE

To examine the role of oxidative and nitrosative stress in the carcinogenesis of Cutaneous T cell Lymphoma (CTCL) through investigating the status of p53 tumor suppressor gene, nitric oxide synthase-2 (NOS2), cyclooxygenase-2 (COX2), nitrotyrosine (NT), hypoxia induced factor- $\alpha$  (HIF- $\alpha$ ), etheno adducts A, C and G and 8-oxyguandine (8-OdG) in these tumor samples.

### TECHNICAL APPROACH

Archival samples obtained from WRAMC were cut and 4 and 8 $\mu$  sections were obtained as outlined in the protocol. So far sixty-six patients with T cell lymphoma and twenty- seven patients with age, gender and duration of disease matched cases with chronic inflammatory diseases have been identified and recruited in the study. 4 $\mu$  thick sections that were mounted on electrically charged glass slides were heated in a drying oven at 60 degrees centigrade for 45 minutes, de-paraffinized in 3 changes of xylene solution and dehydrated in decreasing alcohol grades, for 5 minutes each. Immunohistochemical protocol using strepavidin-biotin methods followed by chromogenic development was performed and completed using antibodies against NOS2, COX2, NT, p53, GxP, MDA, and SOD. MDA marker was added to the protocol since they provide good alternative to ethno A, C, and G, where no good antibodies are available. MDA is a product of lipid peroxidation that binds to DNA nitrogen bases and forms M1G Adducts. GxP and SOD are enzymes involved with scavenging and neutralizing reactive oxygen species. DNA material from 8 $\mu$  sections by Microdissection method has been achieved and DNA extraction using chloroform-phenol methods has been completed, detection of Etheno A, C, G has been achieved using Fourier Transform Infrared spectroscopy (FT-IR).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

We have so far analyzed seventy samples of both CTCL and control. Furthermore, we have contracted Sigma Aldrich to synthesize and to produce altered sequences with known number and location of modified DNA nitrogen bases. So far, we have received oligonucleotide of wild p53 exon 5 and 6 and modified sequences where one, three and six adenine bases have been modified.

The number of subjects enrolled to the study since last APR at WRAMC is 70 and the total enrolled to date at WRAMC is 70.

### CONCLUSIONS

Not provided.

## DETAIL SUMMARY SHEET

TITLE: The Role of Erythropoietin and Erythropoietin Receptor in Thyroid Carcinoma

KEYWORDS: thyroid, cancer, erythropoietin

PRINCIPAL INVESTIGATOR: Francis, Gary COL MC  
ASSOCIATES:

DEPARTMENT: Pediatrics  
SERVICE: Pediatric Endocrinology

STATUS: O  
INITIAL APPROVAL DATE: 19 February 2002

### STUDY OBJECTIVE

To determine if EPO and EPO-R are expressed by thyroid cancer and to determine if EPO/EPO-R expression is related to clinical course of thyroid cancer.

### TECHNICAL APPROACH

Archived, formalin-fixed tissue sections were prepared and stained by immunoperoxidase method for EPO and EPO-R.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 17 and the total enrolled to date at WRAMC is 17. The total number enrolled study-wide is 17, if multi-site study.

A total of 17 samples have been stained for EPO and EPO-R. Of note, EPO and EPO-R are only found in papillary thyroid cancer (not normal thyroid) sections. Tumors with EPO-R are smaller, have lower MACIS scores, and are less likely to recur. The data support the hypothesis that EPO-R expression is a favorable prognostic indicator in childhood thyroid cancer.

### CONCLUSIONS

Tumors that express EPO-R are smaller, have lower MACIS scores, and are less likely to recur. The data support the hypothesis that EPO-R expression is a favorable prognostic indicator in childhood thyroid cancer.

## DETAIL SUMMARY SHEET

TITLE: The Role of Insulin Like Growth Factors in Thyroid Cancer

KEYWORDS: thyroid, cancer, IGF

PRINCIPAL INVESTIGATOR: Gary Francis, COL MC

ASSOCIATES: Andrew Bauer, Aneeta Patel, Michael Tuttle, Timothy O'Neill

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Endocrinology

INITIAL APPROVAL DATE: 18 April 2002

### STUDY OBJECTIVE

To determine if thyroid cancers express IGF and the IGF receptors (IGF-R) and to determine if the tumors that express IGF/IGF-R are more aggressive.

### TECHNICAL APPROACH

Archival, formalin fixed thyroid tumors will be sectioned and stained for IGF-1, IGF-2, and the IGF-R. The intensity of staining will be quantified and correlated with tumor size, extent of disease, and recurrence.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

We have successfully stained 29 thyroid cancers for expression of IGF-1 and IGF-R. Our data show that about half the cancers express IGF-1 (45%) and IGF-R (43%). Of note, tumors that express IGF-R are more likely to recur ( $p=0.05$ ) and to exhibit aggressive features (tissue invasion, distant metastasis, recurrence).

The number of subjects enrolled to the study since last APR at WRAMC is 29 and the total enrolled to date at WRAMC is 29. The total number enrolled study-wide is 29, if multi-site study.

### CONCLUSIONS

Expression of IGF-R appears to be associated with more aggressive tumor behavior, suggesting that the IGF-IGF-R axis is important in thyroid cancer growth and recurrence. This may provide a window of therapeutic opportunity that could be exploited against aggressive disease.

## DETAIL SUMMARY SHEET

TITLE: The Potential Role of Gastric Inhibitory Polypeptide in Obesity and In Cortisol Secretion

KEYWORDS: Obesity, GIP, adrenal steroids

PRINCIPAL INVESTIGATOR: MAJ Andrew J. Bauer MC

ASSOCIATES: Merrily Poth, M.D. and Derek Stocker, M.D.

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Pediatric Endocrinology

INITIAL APPROVAL DATE: 11 December 2001

### STUDY OBJECTIVE

To explore whether the cortisol response to an infusion of 1 microgram (low dose) of ACTH is increased when the ACTH is given with a standard meal. This would suggest that some other food-induced factor is directly stimulating cortisol secretion.

To explore the effect of the degree or type of obesity in relation to the amount of cortisol and/or GIP induced by ACTH with or without a standard test meal.

### TECHNICAL APPROACH

Subjects are given a 1-microgram dose of Cortrosyn IV in the morning after taking 1 mg of Dexamethasone at midnight the night before. This is done twice. Once immediately before drinking a can of Ensure Plus, and once without this test meal. On each occasion, blood is drawn for determination of glucose, insulin, cortisol, GIP, and ACTH at -30 minutes, zero time, +30 minutes, 60 minutes, and 120 minutes.

Comparison is made between the results of the two Cortrosyn stimulations tests. We will also examine the data for correlation between the degree of obesity and the magnitude of the cortisol and GIP responses.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No recent data has been published relevant to the question under study. The number of subjects enrolled to the study since last APR at WRAMC is 6, of which 5 completed the study. The total enrolled to date at WRAMC is 6. This is not a multi-site study.

### CONCLUSIONS

Preliminary analysis of the data to date does not confirm the hypothesis that under the conditions of suppression of endogenous ACTH with Dexamethasone, a test meal will increase the cortisol response to a low dose of ACTH infusion. Larger numbers of subjects may reveal that this does occur in some subjects. The small number of subjects to date does not permit any analysis of the relationship of the degree or type of obesity relative to the magnitude of the hormone response.

## DETAIL SUMMARY SHEET

TITLE: Characterization of Lymphocytic Infiltration in Childhood Thyroid Cancers

KEYWORDS: thyroid, cancer, lymphocytes

PRINCIPAL INVESTIGATOR: Jitu Modi, CPT MC

ASSOCIATES: Francis, Gary, COL MC

DEPARTMENT: Pediatrics

SERVICE: Pediatric Endocrinology

STATUS: O

INITIAL APPROVAL DATE: 22 January 2002

### STUDY OBJECTIVE

To determine the types of lymphocytes present in thyroid cancer and to determine if a specific type of lymphocyte is associated with more favorable outcomes for thyroid cancer.

### TECHNICAL APPROACH

Archived, formalin-fixed tissue sections were prepared and stained by immunoperoxidase method for CD3, CD4, CD8, CD19, and CD56 lymphocyte markers.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A total of 17 samples have been stained for CD3, CD4, CD8, CD19, and CD56. Of note, the majority of thyroid tumors contain a mixture of lymphocytes. Papillary thyroid cancers that contain a mixture of CD4, CD8, and CD19 lymphocytes have the most favorable prognosis. The data support the hypothesis that the immune response against thyroid cancer is important in disease-free survival and that a mixed immune response is important.

The number of subjects enrolled to the study since last APR at WRAMC is 17 and the total enrolled to date at WRAMC is 17. The total number enrolled study-wide is 17, if multi-site study.

### CONCLUSIONS

Papillary thyroid cancers that contain a mixture of CD4, CD8, and CD19 lymphocytes have the most favorable prognosis.

## DETAIL SUMMARY SHEET

TITLE: Correlation of BIS Number and University of Michigan Sedation Scale in Sedated Pediatric Patients

PRINCIPAL INVESTIGATOR: Creamer, Kevin M., LTC MC

ASSOCIATES: Shields, Cynthia H., LTC MC; McCown, Michael, CPT MC

DEPARTMENT: Pediatrics

STATUS: C

SERVICE:

INITIAL APPROVAL DATE: 6 August 2002

### STUDY OBJECTIVE

To correlate the BIS Number with the University of Michigan Sedation Scale in pediatric patients.

### TECHNICAL APPROACH

This is a prospective, observational single blinded study to determine whether there is a correlation between BIS and a validated pediatric sedation scale. After, consent, prior to starting sedation, a pediatric BIS probe or an adult BIS probe is applied to the patient's forehead. Age six is when the manufacturer recommends changing to an adult sensor. The BIS monitor is designed so that no periodic adjustment or calibration is required. The BIS sensor automatically conducts an impedance test on each electrode. The electrode gets a pass if the impedance is below an acceptable threshold. A pass on each electrode will be required to confirm correct BIS placement. After confirmation of correct BIS placement is complete, the BIS monitor is covered so that the BIS number is not visible to the investigator. The Modified University of Michigan Sedation Scale (MUMSS) is performed and documented on the patient prior to starting sedation and every ten minutes thereafter until the patient is ready to be discharged from the sedation unit. After data collection on the first few patients, the MUMSS was modified to add a deeper level of sedation, a foot squeeze, since all of the patients were unresponsive to the foot tickle. When the patient is ready to be discharged, the BIS monitor data is printed out and placed on the data collection sheet. The BIS data is the BIS number occurring immediately prior to the application of the sedation scale. BIS monitor time is the time used for recording all variables. All of the usual sedation unit procedures are followed for each patient. In procedures where the BIS probe would interfere with the study, head CT, or MRI, the BIS probe is placed and the MUMSS started immediately after the procedure is completed and continued until the patient is ready to be discharged from the sedation unit. All data collectors are trained to use the BIS monitor and the MUMSS.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There is no new relevant literature on the subject of pediatric sedation and BIS. There were 405 data sets in 38 patients. The mean age was 5.8 years. There was poor correlation between the BIS score and the MUMSS. Spearman's  $r^2 < 0.25$ . The correlation remained poor when subsets of children  $< 3$  years and  $\geq 3$  years were evaluated. After discussion with the statistician, it was decided that there was no indication that adding more subjects would improve the correlation. We are currently continuing data analysis, pending a download of every BIS data point from the equipment. The BIS tended to underestimate the clinical level of sedation. Forty-four percent of the patients had MUMSS scores indicating deep sedation at some point during their procedure. Fifty percent had BIS scores  $< 60$  during their procedure indicating deep sedation. According to the MUMSS, patients were deeply sedated 27% of the time. Using the BIS data, they were deep 15% of the time.

The number of subjects enrolled to the study since last APR at WRAMC is 38 and the total enrolled to date at WRAMC is 38. There have been no adverse events and no patients withdrew from the study.

### CONCLUSIONS

BIS and MUMSS do not correlate well. Using either the BIS or the MUMSS to judge the level of sedation reveals that a large number of patients reach a deep level of sedation, and that they may spend 25% of the time at this deep level. This finding may have monitoring implications for anesthesia and critical care personnel.

## DETAIL SUMMARY SHEET

TITLE: Clinical Use of the Amplatzer PFO Occluder

KEYWORDS:

PRINCIPAL INVESTIGATOR: Burklow, Thomas R. LTC MC

ASSOCIATES:

DEPARTMENT: Pediatrics

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 3 September 2002

### STUDY OBJECTIVE

The AMPLATZER PFO Occluder is a device is approved by the Food & Drug Administration as a Humanitarian Use Device (HUD) under the Humanitarian Device Exemption regulation. Under HDE regulations, the product may only be used by or on the order of a physician in facilities that have local IRBs. Also, HDE regulations require that physicians intending to use the product inform their IRB of their plans to do so. As this device is approved under an HDE, there is no investigational protocol to follow nor is use of the device considered "research".

### TECHNICAL APPROACH

The AMPLATZER PFO Occluder is a percutaneous, transcatheter, occlusion device intended for the non-surgical closure of patent foramen ovale (PFO) in those patients who have had recurrent cryptogenic strokes despite being on medication to prevent strokes which are due to presumed paradoxical embolism through a patent foramen ovale and who have failed conventional drug therapy. Cryptogenic stroke occurring in the absence of potential phanerogenic cardiac, pulmonary, vascular or neurological sources. Conventional drug therapy consists of a therapeutic international normalized ratio (INR) on oral anticoagulants

1. All procedures will be done with general anesthesia and continuous cardio respiratory monitoring.
2. Cardiothoracic surgery will be apprised in advance with the scheduling of any Amplatzer device patients to provide any surgical back up as necessary.
3. All procedures will be performed with biplane fluoroscopy and transesophageal echocardiogram guidance to optimize proper placement of the device.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

To date, no patients have met the rigid inclusion criteria receiving the AMPLATZER PFO Occluder. However, the primary operator for this procedure, reservist CAPT Donald J. Hagler, of the Mayo Clinic continues to provide quarterly consultations at WRAMC and therefore continued access to the device is requested. Review of the literature shows no trend toward adverse events.

Since there have been no patients enrolled, no adverse events have been recorded.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. Since the Amplatzer PFO HDE Occluder is an FDA approved product, there is not a study. Accordingly, AGA is not collecting data for this product and so do not have any implant figures.

### CONCLUSIONS

Continued availability of the device is requested for clinical use.

## DETAIL SUMMARY SHEET

TITLE: A3961 - Treatment for Infants and Children with Intermediate Risk Neuroblastoma, A Phase III Intergroup CCG/POG Study

KEYWORDS: Infants; children; intermediate risk; neuroblastoma; chemotherapy; radiation therapy

PRINCIPAL INVESTIGATOR: Edwards, E. Glenn, LTC MC

ASSOCIATES: Mosijczuk, A. COL; Crouch, G. LtCol; Merino, M. MAJ; Reddoch, S. MD

DEPARTMENT: Pediatrics

STATUS: O

SERVICE: Hematology - Oncology

INITIAL APPROVAL DATE: 11 December 2001

### STUDY OBJECTIVE

1) Determine that Intermediate Risk Neuroblastoma with favorable biology will have a >90% event free survival (EFS) and survival (S) with a short course of chemotherapy (4 cycles) over 84 days without primary radiation therapy. 2) Determine that intermediate risk neuroblastoma with unfavorable biology will have >90% EFS with a longer course of chemotherapy (8 cycles) over 168 days without primary radiation therapy; 3) further define and evaluate the prognostic importance of other biologic factors in the setting of intermediate risk neuroblastoma and reduced therapy in conjunction with ANBL00B1 (WU #01-66002) and the International Neuroblastoma Risk Group criteria.

### TECHNICAL APPROACH

Patients with a diagnosis of biologically favorable or biologically unfavorable intermediate risk neuroblastoma will be treated with cycles of Cyclophosphamide, Doxorubicin, Carboplatin and Etoposide. Patients with favorable biology will receive 4 cycles, while patients with unfavorable biology will receive 8 cycles, with the cycles given every 3 weeks. Patients presenting with intraspinal neuroblastoma and neurologic deficits will be managed with chemotherapy alone to avoid the use of primary laminectomy (unless determined to be appropriate) or radiation. Radiation therapy will be limited to situations in which there is clinical deterioration despite chemotherapy and/or surgery or the presence of persistent viable disease in patients with unfavorable biology after chemotherapy and second look surgery or partial response (PR) following surgery for local recurrence  $\geq$  3 months after completing initial therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study opened for accrual 1 March 1998; approved at WRAMC on 11 December 2001. The predominant Grade 3/Grade 4 toxicity remains reversible hematological, accounting for 74% in course 1 and 87% in course 2. Cardiac and renal toxicities continue to be rare (<2%) and reversible. There is no difference in the type or frequency of Grade 3/Grade 4 toxicities when stratified according to biology or course. 60 patients have been removed early from protocol therapy or are off study. There have been 15 protocol breaks and 7 patients entered onto new studies. Six patients were ineligible (2 for incorrect diagnosis, 3 for incorrect INSS stage, and one late registration). Six patients have died. Potential benefits to patients include remission of their disease with fewer side effects and life-threatening toxicities associated with chemotherapy and radiotherapy.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 333 as of 29 Oct 02.

### CONCLUSIONS

Study conduct has been acceptable without significant problems associated with the implementation of protocol guidelines. There continues to be no undue or unexpected toxicity concerns. Study should remain open at WRAMC.



## DETAIL SUMMARY SHEET

TITLE:

KEYWORDS:

PRINCIPAL INVESTIGATOR: Edwards, E. Glenn, COL MC

ASSOCIATES:

DEPARTMENT: Pediatrics

STATUS: W

SERVICE:

INITIAL APPROVAL DATE:

### STUDY OBJECTIVE

Study withdrawn.

### TECHNICAL APPROACH

Study withdrawn.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn.

### CONCLUSIONS

Study withdrawn.

## DETAIL SUMMARY SHEET

**TITLE:** Evaluation of the Analgesic Effects of Botulinum Toxin A in Post-Operative Pain and Recovery After Lumbar Spine Surgery

**KEYWORDS:** Botulinum toxin, spine, surgery, analgesic, lumbar

**PRINCIPAL INVESTIGATOR:** LTC Robert J. Labutta MD MC

**ASSOCIATES:** LTC Kevin R. Cannard MD MC, CDR Ross Moquin MD MC, LCDR Marilyn Gates, MD MC, MAJ Marc DiFazio MD MC, WenLiang Yan MD PhD, Ms Robin Howard, Biostatistician

**DEPARTMENT:** Neurology  
**SERVICE:**

**STATUS:** O  
**INITIAL APPROVAL DATE:** 20 November 2001

### STUDY OBJECTIVE

The specific aim of this study is to determine if the preoperative administration of Botulinum Toxin A (BOTOX) into the lumbar paraspinal muscles favorably affects the postoperative period after lumbar spinal surgery.

### TECHNICAL APPROACH

No modifications of original design. Administration of BOTOX/placebo: Botulinum Toxin A (BOTOX, Allergan, Inc.) will be prepared by reconstituting freeze-dried toxin with preservative free 0.9% saline to 100-units/ml concentration. The material will be drawn into a 1 cc-tuberculin syringe and injected through a 27-gauge needle. The reconstituted BOTOX solution is colorless and cannot be distinguished from saline. This solution, like saline, causes no pain when administered intramuscularly. The BOTOX or saline injections will be given at four levels in a total of eight sites using a small (27 gauge) needle (between L1 to S1) bilaterally at the area of anticipated surgery. Each site will receive 40 (Weight < 70kg) or 50 (weight ≤ 70kg) units. The injections will be delivered to the para spinal muscles at the levels indicated above approximately one week prior to the OR date. The total dose of the drug per session will not exceed 400 units in any patient that is well within the acceptable recommended dose range.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A PubMed search using the keywords of either: botulinum and back pain, or botulinum toxin and surgery, revealed no new publications relevant to this study published since the literature review listed in the original protocol. The number of subjects enrolled to the study since last APR at WRAMC is 2 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 2, if multi-site study.

### CONCLUSIONS

The protocol is progressing satisfactorily but enrollment has been slowed by several factors, including the prolonged medical absence of the Research Coordinator, and changes in the investigators.

## DETAIL SUMMARY SHEET

TITLE: Assessment of the Efficacy of Botulinum Toxin A For Treatment of Chronic Neck and Back Pain Secondary To Trauma or Acute Strain

KEYWORDS: Botulinum toxin, spine, lumbar, analgesic, low back pain

PRINCIPAL INVESTIGATOR: Kevin R. Cannard, LTC MC  
ASSOCIATES:

DEPARTMENT: Neurology  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 29 November 2001

### STUDY OBJECTIVE

The aim of this study is to determine the efficacy of paraspinal muscle administration of Botulinum Toxin A (BOTOX) in treatment of chronic back pain secondary to trauma or acute strain.

### TECHNICAL APPROACH

No modifications of original design. Administration of BOTOX. Botulinum toxin A (BOTOX, Allergan, Inc.) will be prepared by reconstituting freeze dried toxin with preservative free 0.9% saline to 100 units/ml concentration. The material will be drawn into a 1-cc tuberculin syringe and injected through a 27-gauge needle. The reconstituted BOTOX solution is colorless. This solution causes no pain when administered intramuscularly. Back paraspinal muscles will be injected with Botulinum toxin A via a tuberculin syringe. In patients suffering unilateral or predominantly unilateral pain, only paraspinal muscles of the affected side will be injected. In patients suffering bilateral low back pain, the drug will be administered bilaterally. If there are any trigger points or local tenderness, the drug will be administered as close as possible to those points. The total Botulinum toxin A dose will be divided among 5 paraspinal sites, L1 through L5, or L2 through S1, depending on pain geography. Each injection site will receive a 40 to 60-unit dose, depending on the patient's weight and muscle mass. The total dose in one injection site will not exceed 500 units (not more than 300U if injected unilaterally).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A PubMed search using the keywords of either "botulinum toxin", "lumbar", or "low back pain" revealed no new publications relevant to this study published since the literature review listed in the original protocol.

No adverse events.

The number of subjects enrolled to the study since last APR at WRAMC is 12 and the total enrolled to date at WRAMC is 12. The total number enrolled study-wide is 12, if multi-site study.

### CONCLUSIONS

The protocol is progressing satisfactorily. Subjects have commented favorably on the results they have experienced. Several subjects have requested continuation of BOTOX therapy after their participation in the study had ended. Enrollment in the study has slowed down due to several factors, including the prolonged medical absence of the Research Coordinator, and the change in Principal Investigators. In addition to referrals, of subjects with low back pain, the study gained several patients with a history of chronic cervical pain and chronic thoracic pain. Unfortunately, they do not meet the inclusion criteria for the study as it stands now. As a result of the noted interest of subjects with cervical and thoracic back pain, it is our intention to broaden the scope of the study with modifications to the original protocol to include subjects with a history of back pain in the cervical and thoracic spine regions. Furthermore, it is felt that the inclusion of these subjects will also allow for a more comprehensive study.

## DETAIL SUMMARY SHEET

TITLE: Assessment of Long-Term Efficacy of Paravertebral Muscle Treatment with Botulinum Toxin A (BOTOX) for Chronic Low Back Pain

KEYWORDS:

PRINCIPAL INVESTIGATOR: Ney, John P., CPT MC

ASSOCIATES: Bahman Jabbari M.D., COL MC

DEPARTMENT: Neurology  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 12 February 2002

STUDY OBJECTIVE:

To assess Long-term efficacy and side effect profile of Botulinum toxin A in chronic low back pain

TECHNICAL APPROACH:

A total number of 60 patients will be studied. Inclusion criteria consist of low back pain of six months or longer, no active serious medical disease, no disease of neuromuscular junction, and not being in any drug study that could impair the neuromuscular transmission. Patients will be treated by paraspinal injection of botulinum toxin A at multiple levels unilaterally or bilaterally. The total dose will not exceed 500units/session. Several clinical rating scales for pain and functional disability will be used (Visual analogue scale –VAS, Oswestry functional scale). The ratings will be documented before treatment, 3 weeks after treatment and thereafter every two months up to 14 months. Clinical and functional improvements will be assessed using conventional statistical methods. All side effects will be asked at each visit and carefully recorded.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

To date a total numbers of 14 patients have been studied. They were 24-76 years of age. Their pain duration ranged from 1-27 years. At three weeks 50% of the patients reported significant pain relief measures by VAS and 64% reported functional improvement. At two months 62% of the patients reported significant improvement both with VAS and functional scales.

The number of subjects enrolled to the study since last APR at WRAMC is 14 and the total enrolled to date at WRAMC is 14.

CONCLUSIONS

This preliminary report shows short-term effectiveness of paravertebral administration of Botulinum toxin A in patients with chronic low back pain. The results of long-term effects should await the completion of the study.

## DETAIL SUMMARY SHEET

**TITLE:** A Pilot Study Using Actigraphy to Assess Functional Severity and Recovery of Motor Limbs in Acute Brain Injury

**KEYWORDS:** Stroke/Diagnostic assessment.

**PRINCIPAL INVESTIGATOR:** LTC Michael Russo

**ASSOCIATES:** Gabriele Feolo, RN, MSN; CPT Ken Kudelko

**DEPARTMENT:** Neurology

**STATUS:** O

**SERVICE:**

**INITIAL APPROVAL DATE:** 9 April 2002

### STUDY OBJECTIVE

This pilot study seeks to determine whether actigraphy has validity in assessing the severity of brain injury and the prognosis for recovery based upon motor activity changes in acute brain injury. Validated clinical scales and actigraphy-data will be correlated to determine potential usefulness of actigraphy in assessing severity and prognosis of brain injury. Specifically, subscales of the Fugl-Meyer motor assessment should have close correlation to activity recorded on the actigraph. Other clinical scales such as the NIH stroke scale, Glasgow coma scale, Galveston Orientation and Amnesia Test, and Rancho Los Amigos Scale will help classify subjects into mild, moderate, or severe category of brain injury and are expected to have moderate correlation to activity recorded on the actigraph.

### TECHNICAL APPROACH

No modification to the initially submitted protocol. This study is an observational study evaluating actigraphy in the measure of motor function. For stroke patients, Fugl-Meyer Motor Performance Test, Functional Independence Measure (FIM), and NIH stroke scale for stroke patients will be used serially throughout the study enrollment period. These clinical scales will be performed at enrollment, day 7, day 14 or discharge from the hospital, whichever is sooner. The investigators, either a neurologist or physical therapist, will administer the Fugl-Meyer Motor Performance Test. Actigraph recordings will be implemented at the time of obtaining informed consent with routine download of the data. All four limbs will have actigraph recording devices placed in the distal aspect of the limb (wrist or ankle). The actigraph device will remain on the subject until the subject is discharged from the in-patient status at WRAMC or the subject has participated in the study for 14 days. Whichever occurs sooner will determine the completion of the study by the subject. Part of the standard plan of in-patient care for stroke patients includes the rehabilitation and/or maintenance of mobility. For that purpose, patients are managed with a therapy plan to regain adequate mobility again. Within this therapy, regimen (but outside passive range of motion activities) adequate time intervals exist for recording actigraphy data on each individual subject. We will also record the times of physical and occupational therapy sessions and exclude those readings from analysis. Please see Figure 2 for the timeline for these measurements. Available neuroimaging findings from the results of standard of care will be recorded as well as rehabilitation regimen and length of treatment. No adverse events. No patients have been enrolled yet.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No relevant changes in the current scientific literature. No patients have been enrolled yet. The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

No conclusions derived yet. No data was collected yet.

## DETAIL SUMMARY SHEET

TITLE: Modafinil in The Treatment of Fatigue in Post-Polio Syndrome

KEYWORDS: Modafinil, Provigil, Fatigue, Post-Polio Syndrome, Polio

PRINCIPAL INVESTIGATOR: LTC William Campbell MD

ASSOCIATES: COL Bahman Jabbari MD, Dr. Erika Poehm

DEPARTMENT: Neurology

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 25 June 2002

### STUDY OBJECTIVE

This is a double blind, crossover trial using a placebo and modafinil (Provigil). The objective of the study is to assess the response of fatigue in a population of PPS patients to modafinil therapy. To further define, the objective is to 1) ascertain whether modafinil is of any benefit in alleviating the fatigue of Post-Polio Syndrome, and 2) investigate the pathophysiology of Post-Polio Syndrome by sleep, electrodiagnostic, immunological, and biochemical assessments.

### TECHNICAL APPROACH

This study will be conducted using modafinil, which has been approved by the FDA for use in narcolepsy. It has not, however, been approved for use for fatigue associated with PPS. Pursuant to AR 40-7, paragraphs 4-12, "Use of an Approved Drug for an Unapproved Indication", this study does not require an IND from the FDA. Additionally, the Department of Health and Human Services "Investigational Use of Marketed Products" guidelines dated February 1989 indicate that an IND number is not required for this study.

One hundred subjects will be recruited for the study. We plan to have about one-third of patients participate at each of the three institutions involved: WRAMC, National Institutes of Health (NIH), and the National Rehabilitation Hospital (NRH). We will recruit up to forty patients who are eligible for medical care at WRAMC (military healthcare beneficiaries). Patients with a history of remote poliomyelitis and a presumptive diagnosis of PPS will be recruited. After obtaining informed consent, the first step will be to administer the fatigue instruments (FIS, FSS, VAS-F, ESS, and BDI-II). Subjects with a FIS score of >75 who do not have clinically significant depression or EDS will continue. Patients will then undergo general medical and neurologic evaluations to ensure that the diagnosis of PPS is correct and to exclude any coexistent conditions that might be causing enough fatigue to interfere with interpretation of the study. They will begin a sleep diary to help assess for sleep disorder and sleep hygiene patterns. The investigators may examine the patients' past medical records. An electrodiagnostic evaluation will be carried out if a previous electrodiagnostic evaluation has not resulted in an unequivocal diagnosis of PPS. Patients who are judged to have PPS, a significant problem with fatigue, and no confounding medical condition will have screening lab work and EKG performed. (Exclusion criteria are outlined in protocol and blood drawing.) If these are normal, the patient will undergo sleep studies to exclude a sleep disorder that might be the cause of their fatigue. Following the sleep studies, subjects who qualify to continue for the treatment phase, and are willing, will then undergo an optional lumbar puncture. Patients who enter the treatment phase of the study will then be randomized to begin treatment with placebo or modafinil. There will be an equal number of subjects in each treatment sequence. Randomization will be determined using a computer program based on random number generation. All researchers and patients will be blinded to the order of treatment. A research coordinator will be the only person in the study who will know the type of treatment. There will be a modafinil phase and a placebo phase. Each phase lasts six weeks and is separated by a two-week washout period. This washout period should suffice, since modafinil is cleared with a half-life of about 11-14 hours and reaches steady state after three daily doses. On the day of initial intervention (start

of the treatment phase), the patient will have cytokine levels drawn along with blood for viral testing. For the first three weeks of the modafinil phase, the patient will take one tablet of modafinil (200mg) at breakfast and a placebo tablet four hours later for a total daily dose of 200mg. Starting with the 200mg dose will decrease possible dose related side effects and help assess the response to a sub maximal dose of the drug. This design is similar to a study used for modafinil in the treatment of EDS in narcolepsy. For the next three weeks of the modafinil phase, the afternoon tablet will also be modafinil, for a total daily dose of 400mg. For the placebo phase of the study, the patient will take the placebo twice daily, with one tablet at breakfast, and one tablet four hours later. Patients will be issued study medication at the initial visit of each treatment phase.

Assessment will be done at three and six weeks from the initial date of each treatment phase (weeks 3, 6, 11, and 14), to include interview, VAS-F, FSS, FIS, BDI-II, ESS, and review of the sleep diary. Patients will also have blood drawn for cytokine levels at weeks 6, 8, and 14. The data will be assessed to search for any changes in the symptoms of fatigue between the placebo and treatment phase of the trial and whether any benefit that might occur is a nonspecific effect that correlates with improvement in depression or EDS. If there is benefit, the analysis will seek to detect any difference between the 200mg and the 400mg doses of modafinil, and any differences in response for patients with greater and lesser degrees of fatigue based on initial FSS score (see sample estimation).

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

An addendum was submitted to utilize a patient information sheet for patient education in February 2003. The phone number on the approved recruitment poster was changed to incorporate a toll free number for patient access in February 2003. Both items had recommended changes and were forwarded back to WRAMC DCI approval 21 April 2003.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

#### CONCLUSIONS

Since this is a multi-site study requiring a great deal of patient coordination and involving medication dispensation, blood work, and testing, no patients have been enrolled to date. We did receive secondary concurrence from USUHS on 28 October 2002. The protocol was approved by the Medstar Institutional Review Board for National Rehabilitation Hospital effective 25 February 2003. The study has also been submitted to both the USUHS and NIH for approval of research at those sites. These actions are still pending and approval at both sites is expected shortly.

## DETAIL SUMMARY SHEET

**TITLE:** A Randomized, Placebo-Controlled Trial of Sertraline for Chronic Neurobehavioral Sequelae of Traumatic Brain Injury

**KEYWORDS:** traumatic brain injury, head injury, SSRI

**PRINCIPAL INVESTIGATOR:** Warden, Deborah L. M.D. DAC

**ASSOCIATES:** Kara S. Comins BS, LTC(P) James Ecklund MC, Maria E. Graves RN, COL Robert Labutta MC, Elisabeth Moy Martin RNC MA, Laurie M. Ryan Ph.D., Karen Schwab Ph.D., Molly B. Sparling BA, Joan Walter PA

**DEPARTMENT:** Neurology  
**SERVICE:**

**STATUS:** O  
**INITIAL APPROVAL DATE:** 25 June 2002

### STUDY OBJECTIVE

To investigate the efficacy of Sertraline, an SSRI, in treating irritability, depression, frustration, anxiety, and other chronic post concussive symptoms following TBI.

### TECHNICAL APPROACH

As the standard of care for patients with traumatic brain injury (TBI) at Walter Reed, patients receive a multidisciplinary evaluation consisting of neurology exam, neuropsychology, psychiatry, psychosocial, EEG, MRI, phlebotomy, and family interview. Research tests include drawing and storing of the blood sample and some questionnaires related to the subject's medication response. Blood samples (about two tablespoons) are kept at the Defense and Veteran's Head Injury Program (DVHIP) labeled with the patient's study number for possible future use in studies to better understand aspects of recovery from head injury. Blood samples are used in studies of genetic markers potentially related to outcome from TBI. Participants have the option of not consenting to the genetic analyses while still participating in the rest of the protocol. After being screened for eligibility and signed the volunteer informed consent form for the current Sertraline protocol, the tests and scales will be administered and patients will be randomized into treatment group A (Sertraline or placebo up to a dose of 200 mg of Sertraline or 4 tablets of placebo). This initial treatment period will be followed by a three-week washout period and then the alternate treatment for twelve weeks. Patients will receive standard TBI care during this period. Current standard of care for patients with moderate-severe TBI following a full evaluation with medical/surgical treatment of any acute medical/surgical conditions is approximately eight weeks of Convalescent Leave Home (CVL) followed by a gradual return to duty. Mild TBI patients typically receive 1-4 weeks of CVL followed by a gradual return to duty. Civilians would have similar schedules for resumption of activities. All patients are contacted weekly during the 27-week treatment phase to assess general condition, current symptoms, and assessment of compliance.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no addenda or adverse events to date.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. A literature search on 7 April 2003 yielded two recent articles on SSRIs and traumatic brain injury, but nothing examining post concussive symptoms.

### CONCLUSIONS

Recruitment has been put on hold due to the large number of research projects going on in the DVHIP. We do anticipate recruiting subjects in the future.



## DETAIL SUMMARY SHEET

TITLE: Telemedicine Assessment of Neurobehavioral Consequences of Traumatic Brain Injury

KEYWORDS: Traumatic Brain Injury, Post Concussive Symptoms, Telemedicine

PRINCIPAL INVESTIGATOR: Warden, Deborah L., M.D., DAC

ASSOCIATES: Kara S. Comins, BS; Elizabeth Moy Martin, RNC, MA; COL Robert J. Labutta, MC; Thomas Boal, PhD; Laurie M. Ryan, PhD; Molly Sparling, BA

DEPARTMENT: Neurology  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 30 July 2002

### STUDY OBJECTIVE

The objective of this project is to provide a brief screen of common symptoms experienced by individuals who have sustained a traumatic brain injury (TBI).

### TECHNICAL APPROACH

This project utilizes telemedicine technology already established within the WRAMC Telemedicine Department. A website will be established with the following on-line research evaluation tools: The Post Concussive Symptom Checklist (Gouvier-PCSC) is used to assess the frequency, intensity, and duration of common post-concussive symptoms, The Cicerone Post-Concussive Scale is used to assess common symptoms experienced following TBI, The Beck Depression Inventory-II is a self-report scale of depressive symptoms, and The State-Trait Anxiety Inventory (STAI) is a self-report inventory of situational and trait anxiety symptoms. A registry form will be used to document demographic and injury characteristics such as severity called The Automated Neuropsychological Assessment Metrics, which is a cognitive screening tool to be utilized in this project. All computerized assessments will be reviewed immediately upon completion for discrepancies that may affect clinical care. If a patient endorses suicidal ideation, our psychiatric research nurse and study physician will immediately evaluate them. If the ideation is confirmed, the patient will be referred to inpatient psychiatry. Otherwise, these forms will not be used for clinical purposes. ANAM and traditional neuropsychological tests used in concussion research have been shown to have significantly similar factor structures. The ANAM has successfully been used in the Defense and Veterans Head Injury Program (DVBIC) study of sports concussion at West Point. The ANAM battery employed in the present study consists of the following sub-tests: The 'Stanford' Sleepiness Scale/Mood Scale-2R Scales, Simple Reaction Time, and Continuous Performance Task. These tests were found to be most sensitive to change after concussion in the West Point Study. The ANAM has already been successfully implemented in a Walter Reed Psychology telemedicine study of pilots. Individuals who consent to participate in the protocol will receive in-person standard of care tests and computerized versions at least one day, but no greater than three days apart. Participants will be assigned at random to one of the two sequence groups to ensure an equal number of participants in each group.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

A recent literature search revealed two recent publications focusing on telemedicine and brain injury, but no new research directly relating to this protocol. There are two recent publications focusing on telemedicine and brain injury, but no studies looking at a comparison of assessments and post-concussive symptoms like this. Two participants did not return to complete their paper evaluations and one participant did not return to complete the web assessment. Two of these individuals had scheduling conflicts, which made them unable to return within the 24-72 hour time interval. One of these patients never returned for the scheduled paper evaluation for reasons unknown. The number of subjects enrolled to the study since last APR at WRAMC is 24 and the total enrolled to date at WRAMC is 24

### CONCLUSIONS

We feel that the protocol is running smoothly and there have been no adverse events related to the protocol to date.

## DETAIL SUMMARY SHEET

TITLE: Enhanced Head Protection for Paratroopers – Efficacy of Countermeasures Against Traumatic Brain Injuries Sustained in Airborne Operations

KEYWORDS:

PRINCIPAL INVESTIGATOR: Warden, Deborah L., M.D. DAC  
ASSOCIATES:

DEPARTMENT: Neurology  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 3 September 2002

### STUDY OBJECTIVE

To determine the effect of helmet configuration on the head injury incidence rate as experienced by an operational airborne unit.

### TECHNICAL APPROACH

This study is being conducted by the US Army Aeromedical Research Laboratory (USAARL) in collaboration with the Defense and Veterans' Brain Injury Center (DVBIC) and Womack Army Medical Center (WAMC). Fort Bragg is the data collection site. Fort Rucker is the study management site. WRAMC is the data management and analysis site.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study is progressing more slowly than anticipated due to inexpertly slow IRB approvals from several different institutions, and most recently, due to the planned subject population being deployed OCONUS for the past several months. Nonetheless, the entire study infrastructure is in place and limited subject recruitment is progressing. We have determined that an additional two years of data collection will be required to achieve the statistical power needed to discriminate among the experimental groups, if a true difference in head injury reduction is present. Funding for these two years has been tentatively identified.

The number of subjects enrolled to the study since last APR at WRAMC is 118 and the total enrolled to date at WRAMC is 118. This is not a multi-center trial.

### CONCLUSIONS

There are no results to report at this point, except cohort demographics. There have been no adverse events so far. There have been no recent reports concerning helmet performance to our knowledge. We are aware of a recently initiated study comparing different football helmet types in the Pittsburgh high school system. Contacts have been made with the investigators. Two amendments have been submitted in the last month that update administrative details and procedures. They are currently being reviewed by the IRBs.

## DETAIL SUMMARY SHEET

TITLE: A Study of the Use of Telemedicine/Teleradiology Consultation in Acute Strokes, Part II

KEYWORDS: stroke, NIH stroke scale, Telehealth, urgent care

PRINCIPAL INVESTIGATOR: Urban, Edward, M.D. DAC

ASSOCIATES: LTC Geoffrey Ling MC, COL Robert Labutta MC, COL Ronald Poropatich MC, LTC Edward Lucci MC, LTC Dianna Chooljian MC, Gabriele Feolo, RN MSN

DEPARTMENT: Neurology  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 3 September 2002

### STUDY OBJECTIVE

To establish the validity of remote telemedicine consultation by a neurologist in the diagnosis of stroke. Accuracy of the final diagnosis, brain computed tomography (CT) interpretation, and telemedicine consultation time use will be examined. To present evidence that neurologists will be able to use telemedicine technology to provide accurate acute stroke consultation within an acceptable time frame.

### TECHNICAL APPROACH

This is a prospective multi-center study designed to evaluate the validity of telemedicine interventions in the initial management of acute ischemic stroke. We will use simulated patient ER ED encounters. An analysis will be made of real time telemedicine consultation including the accuracy of neurological diagnosis and the overall time used for arriving at this final neurological diagnosis. No changes or amendments were made to the protocol since the receipt of the approval letter by the DCI on 3 September 2003.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

No changes in the protocol.

LaMonte et al describe Telemedicine as an emerging potential timesaving, efficient means for evaluating patients experiencing acute stroke. In areas where local stroke care specialists are not available, telemedicine can link an ER physician with a specialist in a stroke treatment center. This consultation provides an opportunity for administration of thrombolytic drugs within the short therapeutic time window associated with ischemic stroke. In their 2003 publication examples from a Maryland stroke treatment center and reports of safe administration of recombinant tissue plasminogen activator (rtPA) during telemedicine consultation are discussed.

The 2003 Maulden publication addresses the impact of information technology and the Internet on the current and future practice of neurology. Information technology is influencing medical practice in ways that could be both beneficial and harmful. Scenarios are presented to depict some of the ways in which the practice of neurology is being influenced by the growth of technology.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

Continue to attempt to recruit a collaborating site as a remote consultant for the study's execution.

## DETAIL SUMMARY SHEET

TITLE: Evaluation of the Effect of a WEB BASED Automated Mental Health Intake System on Parent/Guardian Satisfaction and Discussion Provider's Response

PRINCIPAL INVESTIGATOR: Chun, Ryo Sook COL MC  
ASSOCIATES: Cozza, Stephen LTC(P) MC, Sarah Rosquist

DEPARTMENT: Psychiatry  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 19 February 2002

### STUDY OBJECTIVE

This is a feasibility study. The feasibility of using a web-based automated intake system and automated report writer in the Child and Adolescent Psychiatry Clinic will be ascertained by addressing the following objectives: Determine how satisfied parent/guardians are with the Web-Based Automated Mental Health Intake System (WAMHIS) when compared to parents using the standard manual (paper-based) intake system. Determine how satisfied providers are with WAMHIS versus the manual system. Explore whether the clinical data gathered via WAMHIS is as comprehensive and thorough as that gathered in the traditional method. Identify problems encountered by parents and providers when using WAMHIS. Examine how satisfied providers are with the computer-generated reports, and how the system affects providers' ability to do write-ups.

### TECHNICAL APPROACH

Parents of new patients are sent an information packet at home at least one week prior to their appointment. The packet contains the consent form, explanatory letter, and an informational packet. Parents are called at least two days prior to their initial appointment and are asked if they would be interested in participating in the research study. If interested, parents are assigned to one of three groups. Those research participants assigned to group 1 are asked if they have questions about the consent form, and are instructed to sign the consent form prior to completing the intake forms on-line at home. Those research participants assigned to group 2 or 3 are asked to come to the clinic one hour before their appointment to be consented before they complete the intake forms on the computer or using paper and pencil. After all three groups have completed the intake forms, they complete Parent Survey 1. If parents assigned to group 1 do not complete the intake forms at home, they are reassigned to group 2 or 3, and given an additional survey called 1A. After the parents have completed the intake interview with their provider, they are given Parent Survey 2.

Providers participating in the survey are consented once at the beginning. When providers are seeing a patient who is also participating in the study, the providers are given one survey after the interview and one survey after they complete their report. Initially, they also complete a longer survey after their initial report using WAMHIS. At the end of the study, the providers will complete a final survey after their last report using WAMHIS.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 5 and the total enrolled to date at WRAMC is 5.

### CONCLUSIONS

Data collection is slow. We have encountered the following problematic areas: difficult to reach parents at home on the telephone, parents assign themselves to groups, cancelled appointments, too little time to send out packets to parents before appointments, and parents are not listed in CHCS.

We will be changing research assistants in January 2003. To prepare for the transition, we have interviewed several candidates and identified a replacement. We are also preparing data entry forms on Access. Additionally, we are cataloguing all computer files. No adverse events in past year. No recent literature.

## DETAIL SUMMARY SHEET

TITLE: A Demonstration Project – Description of Well-Being and Satisfaction in Subjects Assigned to Follow-Up Psychiatric Treatment in the Traditional Approach Versus a Telemedicine Approach

PRINCIPAL INVESTIGATOR: Wain, Harold J., Ph.D. DoD

ASSOCIATES: LTC(P) Stephen J. Cozza, MC, MAJ(P) John Staisinos, MC, LTC(P) Charles Milliken, MC, MAJ(P) Geoff Grammer, MC, Ms. Corina Miller, Ms. Catherine DeBoer

DEPARTMENT: Psychiatry  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 26 February 2002

### STUDY OBJECTIVE

To describe the well being and satisfaction in subjects assigned to either a traditional approach of receiving follow-up psychiatric treatment or a telemedicine approach to follow-up psychiatric treatment.

### TECHNICAL APPROACH

This demonstration project utilizes an exploratory study design in which subjects are randomly assigned to one of two groups. Group one receives the standard of care consisting of the patient returning to their community and receiving follow-up “as needed”. Group two also returns to their community, however, they receive follow-up through scheduled VTC/telemedicine.

Following the initial clinical evaluation of patients referred to PCLS at Walter Reed, eligible patients are approached by the research assistant and asked to participate in the study. Patients who consent to participate in the study are briefed and informed consent is obtained. Each patient will be randomly assigned to either the telemedicine (VTC) group or the standard of care follow-up group. Groups are stratified by medical condition and randomized. After completing the consent form, each participant completes the General Well-Being Schedule, a demographic form, and the Client Satisfaction Questionnaire. Patients receiving extended care (remain hospitalized or receive further medical or psychiatric treatment) at WRAMC, complete both the General Well-Being Schedule and the Client Satisfaction Questionnaire again prior to the patient’s discharge from WRAMC. Upon treatment completion at WRAMC, patients return to their communities to receive follow-up care for eight weeks. (Though follow-up may continue, patients only participate in the study for eight weeks.) Typically, PCLS clinicians maintain contact with patients referring physicians. Patients assigned to the telemedicine group are treated by one of the psychiatry liaison doctors from the team of doctors they received treatment from at WRAMC, and, when appropriate, from their referring physician. VTC appointments take place in a locked room. The research assistant provides assistance to the WRAMC staff member with start-up of the telemedicine equipment at WRAMC. The assistant then leaves the room while the conference is in session. There is a VTC technician or VTC proficient clinician who assists the patient with set up at the other telemedicine sites. This person also leaves the room during the conference, but remains nearby in case of technical problems. Only the WRAMC staff member and the patient are present during the conference. Patients have a VTC appointment every week, for a total of eight VTC appointments. Following each appointment, the research assistant contacts the VTC group to complete the General Well-Being Schedule and the Client Satisfaction Questionnaire over the phone. (Subjects receive a copy of these to refer to during the phone calls.) In addition, the VTC group is also asked to provide information regarding medication used and additional medical care sought. Each phone interview lasts about 10-15 minutes and is scripted. All patients are also given information about signs and symptoms indicating decompensation, and instructions to call the research assistant should they experience any of the listed symptoms. If the research assistant is called for this reason, the PCLS doctor who treated the patient will be notified. The research assistant scores the Well-Being Schedule after each phone interview, and notifies the PCLS doctor treating the patient if the score indicates severe distress.

The standard-of-care group returns to their communities without scheduled appointments with local mental health personnel. Standard procedure dictates that a referral for follow-up is given to patients and the patient is expected to

make the appointment. Patients may or may not have a scheduled appointment with their primary care doctor. The results of the initial PCLS evaluation are forwarded to the referring physicians and contact between the physicians is maintained. If problems increase, patients are instructed to call the primary physician or emergency room, or consult a local mental health provider. Although patients in this group may receive different types of follow-up medical care, it is assumed to be randomized across all groups. Though PCLS is monitoring all psychological-psychiatric care given to the VTC group, the standard-of-care group may or may not receive psychological-psychiatric care. If patients in the standard-of-care group receive psychological care, it is also assumed to be randomized and will not be given by WRAMC PCLS. The standard-of-care patients are contacted every week to complete the General Well-Being Schedule and Client Satisfaction Questionnaire over the phone, as well as provide information regarding medication used and additional medical attention sought. (Patients receive a copy of the Schedule and Questionnaire to refer to during the phone calls.) Each phone call lasts 10-15 minutes and is scripted. Patients requesting additional care after completing the study will be provided with scheduled follow-up visits via VTC or in-person at WRAMC.

This demonstration project lasts for a total of eight weeks. Additional treatment provided, if needed after the eighth week, will be outside the methods of this demonstration project. Only data collected at baseline, following extended treatment (if needed), and through weekly phone calls will be used in this project. There have been no modifications made to the methodology of this project since its initial approval.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Four subjects have enrolled in the study since February 2002. One has completed the study, one is in the third week of the study, and two have recently consented but have yet to begin. Additional patients have been approached and briefed. Among the patients enrolled in the study, none have withdrawn at the time of this reporting.

Approval is still being sought to include additional bases in the study. Access to these bases will provide a larger population of subjects eligible for the study and thus expedite the recruitment process.

There have been no expected or serious adverse events as a direct result of this study. There has not been any literature review since the beginning of the study.

The number of subjects enrolled to the study since last APR at WRAMC is 4 and the total enrolled to date at WRAMC is 4.

#### CONCLUSIONS

At this time no conclusions can be determined regarding the well being and satisfaction among patients assigned to follow-up psychiatric treatment through either the traditional approach or the telemedicine approach.

## DETAIL SUMMARY SHEET

TITLE: A Multi-Center, Prospective Study on Pediatric Seasonal Affective Disorder (SAD) Incidence

PRINCIPAL INVESTIGATOR: Morris, James MAJ MC

ASSOCIATE: Ruth E. Edelman, PhD

DEPARTMENT: Psychiatry

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 25 June 2002

### STUDY OBJECTIVES

1. Estimate the proportion of children and adolescents in Washington DC and Honolulu HI who have Seasonal Affective Disorder (SAD).
2. For each site, compare the change in SIGH-SAD scores between winter and summer.
3. Compare the winter and summer SIGH-SAD scores between Washington DC and Honolulu HI.
4. Identify cases of clinically significant depressive disorders, including Seasonal Affective Disorder, in a pediatric population and offer treatment to these subjects.

### TECHNICAL APPROACH

Subjects between the ages of 5 and 18 will be recruited to participate in this study from the general pediatric clinics at Walter Reed Army Medical Center and Tripler Army Medical Center. Parents and/or guardians will receive a description of the study along with a statement of interest upon which they may provide their address and phone numbers. The principal investigator will contact the parents by phone to arrange a one-time clinic visit for the purpose of answering any further questions and obtaining informed consent for enrollment. The designated principal investigator at each site will obtain assent from subjects between the ages of 12 and 18 years by having them sign on the designated space on the assent form. Once enrolled, the parents and their children (the study subjects) will be contacted by telephone twice in a year – once in January and again in July. Each sampling period will last four weeks. The investigator contacting the parent will administer the SIGH-AD-P over the telephone, and if possible, also administer at that time the SIGH-SAD-C to the child. If the child is unavailable for questioning at that time, the telephone interview with the child may be conducted at a later time during the four-week sampling period. The end point for each subject is the acquisition of parent and child data for two seasonal sampling periods (July and January).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled in the study since last APR at WRAMC and TAMC is 0 and the total enrolled to date is 0.

### CONCLUSIONS

Data collection has not been initiated since protocol approval (14 February 2003).

## DETAIL SUMMARY SHEET

**TITLE:** The Impact of Group Psychosocial Intervention on Quality of Life for Breast Cancer Patients and Their Partners – A Pilot Study

**KEYWORDS:** Breast cancer, psychosocial support, group psychotherapy

**PRINCIPAL INVESTIGATOR:** LTC Debra Dunivin MC

**ASSOCIATES:** COL Craig D. Shriver MC, LTC George E. Peoples Jr., MC, CPT Joseph Flynn MC

**DEPARTMENT:** Psychology

**STATUS:** O

**SERVICE:**

**INITIAL APPROVAL DATE:** 25 June 2002

### STUDY OBJECTIVE

1. Determine the feasibility of implementing a standardized program of brief psychosocial group interventions for both breast cancer patients and their partners. For the purposes of this study, partners are defined as legal spouses who are DoD beneficiaries.
2. Identify a set of measures of psychosocial functioning and quality of life that may be used to assess the outcomes of these interventions in a larger subsequent study.

It is expected that this pilot program will facilitate development of hypotheses for subsequent research investigations. Furthermore, proof of this concept will provide the necessary insight into the efficacy and feasibility of greater implementation into the therapeutic armamentarium available to healthcare providers caring for patients with breast cancer. Feasibility of the intervention program will be determined based on the reproducibility of the interventions at different sites with different providers. The program is also expected to provide valuable insights into the potential clinical benefits over a longitudinal surveillance/treatment period. Finally, direct input by the patients and providers will be obtained in order to score their satisfaction with the program. This will provide the needed modeling insights required for change in future endeavors.

### TECHNICAL APPROACH

The clinical interventions used in this study are part of a psychosocial support group program that was implemented in April 2002. The program was developed through a fifteen-month collaboration of the WRAMC Department of Psychology, the Clinical Breast Care Project, and the American Psychological Association in consultation with Winder Medical Center and the Tom Baker Cancer Centre. These group interventions are considered standard of care in the WRAMC Clinical Breast Care Project. The questionnaires that have been used for the research study are the same outcomes measures used to assess clinical effectiveness and participant reactions to the group program. Patient and partner groups have and will continue to be scheduled approximately every two months, with each group containing between five and ten participants, depending on the rate of participant accrual.

The initial participants enrolled in this study were seen in a group offered at the Department of Behavioral Health, DeWitt Army Community Hospital, Fort Belvoir, VA beginning 13 November 2002 and facilitated by the PI and collaborating personnel. Healthcare providers who were interested in becoming group facilitators were identified and subsequently trained. These providers have considerable experience working with medically ill patients and are aware of the varying dynamics of patients based on such factors as staging and phase of illness, type of treatment, and psychosocial factors. Their training as group facilitators began with a two-day workshop and continues with subsequent weekly supervision while facilitating the groups. Participants in both the patient and partner groups being led by these trained facilitators have been enrolled in the study.

The clinical intervention currently being offered is as described in the protocol and addendum. The group location has been modified by adding DeWitt ACH as a site. For the WRAMC participants, rather than



conducting all the groups in the CBC or the TV studio, some have been conducted in the Department of Psychology conference room and 6Z80. This modification allows participation in the group by patients and partners who are unable to be physically present for the sessions but able to participate by VTC. Use of these rooms also allows unobtrusive videotaping of sessions for supervisory purposes as noted in the consent forms. The VTC group participants have not been enrolled in the present study; however, an addendum will be submitted to permit enrollment of VTC participants in the future. No changes have been made to procedures for data collection/analysis.

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 5 and the total enrolled to date at WRAMC is 13. It is noteworthy that more group members are willing to participate in the research project than have been enrolled. For example, of six members currently attending the women's group who wished to participate in the project, only three met inclusion criteria. No adverse events have been reported or observed. Recent literature has supported the previously reported findings that positive-focus coping strategies enhance emotional well-being in patients with breast cancer and that these interventions should be promoted in treatment programs.

#### CONCLUSIONS

Pending completion of study.

## DETAIL SUMMARY SHEET

TITLE: Intravenous Site Selection and Its Role in Reducing Propofol Injection Pain

PRINCIPAL INVESTIGATOR: Mitzak, Anne CPT AN

ASSOCIATES: CPT David Carter, CPT Jennifer Coyner, CPT George Nelson

DEPARTMENT: Nursing  
SERVICE:

STATUS: C  
INITIAL APPROVAL DATE: 15 January 2002

### STUDY OBJECTIVE

To determine if there is a difference in reported pain scores when subjects receive propofol intravenously in the dorsum of the hand versus intravenously in the antecubital fossa.

### TECHNICAL APPROACH

Thirty-four subjects were obtained by using a convenience sample of health ASA I patients who were scheduled for elective surgery at WRAMC. All subjects were informed of the fact that they could participate in the study by virtue of their health status, scheduled surgery at WRAMC, and that part of their anesthetic plan included the administration of the drug propofol. The consent form was reviewed with the potential subjects, inclusion/exclusion criteria were identified, demographic data collected, the verbal descriptor scale (VDS) explained. If the individual wished to take part in the study, informed consent was obtained. All questions were answered prior to the subject signing the consent form. At that point, an intravenous catheter was placed either in the dorsum of the hand or the antecubital fossa. The intravenous catheter site was predetermined by a randomization schedule obtained from the Department of Clinical Investigation (DCI). Standard of care was maintained in that midazolam premedication (anxiolytic) was administered, all standard monitors were applied upon entry into the operating room, and pre-oxygenation was delivered in the standard fashion. Prior to administering the propofol, the intravenous line roller clamp was opened maximally to administer fluids at a standard flow. The IV pole was also standardized at a height of 80 inches. At that time, a 50mg dose of propofol was administered via the intravenous catheter, and the subject reported either a zero, one, two, or three to coincide with the VDS of no pain, some pain, moderate pain, or severe pain, respectively. The investigators also documented the presence or absence of facial grimace and/or arm withdrawal. Once the subject responded according to the VDS, his or her participation in the study was complete. At that time, the investigator continued with the course of the anesthetic as planned. No modifications to the methodology were required.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Data collection was completed on 29 June 2002. Data have been analyzed. Thirty-four subjects were obtained, and no subjects were attrited. No adverse events occurred. Data analysis suggest subjects who receive propofol via an intravenous catheter in the antecubital fossa report significantly less pain than do subjects who receive propofol via an intravenous catheter in the dorsum of the hand. No recent literature has been noted in the area of propofol injection pain as it relates to intravenous site selection. Results of this study will add to the body of research that currently exists on this matter, and, in our opinion, provides anesthesia providers with a simple technique to reduce the pain that patients report when they receive propofol. The number of subjects enrolled to the study since last APR at WRAMC is 34 and the total enrolled to date at WRAMC is 34.

### CONCLUSIONS

Findings of this study suggest that patients who receive propofol via an intravenous catheter placed in the antecubital fossa report significantly less pain than do patients who receive propofol via an intravenous catheter in the dorsum of the hand. Further, significantly fewer subjects demonstrated facial grimace when they receive propofol via an intravenous catheter in the antecubital fossa. Fewer subjects who had an intravenous catheter in the antecubital fossa demonstrated arm withdrawal (although not statistically significant) than subjects who had an intravenous catheter in the dorsum of the hand. Further, females in this

Work Unit # 02-75011 [*Continued*]

study reported more pain than did males, regardless of the intravenous site. We recommend further research investigating the differences in reported pain by males and females. Upon completion of this study, the investigators have several recommendations. We recommend a duplication of this study with a larger sample and a more diverse subject population to include various ethnic and cultural backgrounds. We recommend a follow-up study to further examine our theoretical framework that release of bradykinin is involved in the pain experienced by the subjects. Evaluating serum bradykinin levels following administration of propofol could provide more scientific rigor to this study. Finally, the investigators recommend that anesthesia providers place intravenous catheters in or near the antecubital fossa if propofol is going to be administered. This appears to be an effective, simple technique to reduce the reported pain following intravenous administration of propofol.

## DETAIL SUMMARY SHEET

TITLE: The Relationship of Job Stress to Job Satisfaction and the Intent of Army Nurse Corps Officers to Stay in Active Military Service

KEYWORDS: stress, job satisfaction, intent to stay

PRINCIPAL INVESTIGATOR: LTC Laura R. Brosch MC

ASSOCIATES: LTC Della W. Stewart, Dr. James Vail

DEPARTMENT: Nursing

STATUS: C

SERVICE: Nursing Research

INITIAL APPROVAL DATE: 5 February 2002

### STUDY OBJECTIVE

What is the job stress level experienced by Army nurses? What is the relationship between personal characteristics and job stress? What is the job satisfaction level of Army nurses? What is the relationship between job stress, job satisfaction, and intent to stay in active military service?

### TECHNICAL APPROACH

A random sample of Army nurses was taken from two Army medical centers and six community hospitals in the United States. Information was obtained via using a demographic data sheet, the Nursing Stress scale, the Index of Work Satisfaction, and Price's Intent to Stay Questionnaire. These instruments were mailed to the participants. Fifty-four percent usable surveys were returned via US postal system. Data analysis consisted of descriptive statistics, t-test, Pearson's Product Moment correlation, and one-way Analysis of Variance.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The last literature search was completed 1 August 2002. The results are contained in the protocol. Now new information was found. There were no adverse events.

The number of subjects enrolled to the study since last APR at WRAMC is 37 and the total enrolled to date at WRAMC is 37. The total number enrolled study-wide is 136, if multi-site study.

### CONCLUSIONS

All data collection activities were completed May 2002. Entire study completed 6 August 2002. Level of stress was expressed as between occasional and frequent. No relationship between level of stress and organization type. Position, age group, rank, gender, number of dependents, and time in service were not statistically related to stress. Nurses assigned to MEDCENS reported higher levels of stress than nurses assigned to MEDDACS. Respondents were weakly satisfied with their job. There was a positive relationship between job satisfaction and job stress. There was no statistical relationship between stress, job satisfaction, and intent to stay in the military.

## DETAIL SUMMARY SHEET

TITLE: Providers' Evaluation of Alternative Medications Use By Patients

KEYWORDS: alternative medicine

PRINCIPAL INVESTIGATOR: Patrician, Patricia A. LTC AN

COLLABORATING PERSONNEL: David W. Seiffert, MAJ, AN; Eugene Levine, Ph.D.; Wayne Jonas, MD, LTC, (Ret) MC; Diane Seibert, FNP, RN; Fredric Lombardo, Pharm, D., M.S., R.Ph.

DEPARTMENT: Nursing  
SERVICE:

STATUS: C  
INITIAL APPROVAL DATE: 5 February 2003

### STUDY OBJECTIVE

Determine whether or not primary care providers in the military health care system are actively assessing patients' use of "alternative medications". Examine primary care provider attitudes toward alternative medications.

### TECHNICAL APPROACH

This prospective descriptive study used web-based technology to survey primary care providers about their attitudes and patient assessment behaviors concerning alternative medications. Providers were sent an e-mail advertisement. They were sent to General Internal Medicine physicians, Family Practice physicians, Family Nurse Practitioners, residents, and physician assistants. A web page was developed with the questionnaire integrated into the page. As the providers complete the form, the data were compiled within the "Test Pilot" program. The "Test Pilot" program allowed the development of questionnaires, surveys, and quizzes on an internet web page. USUHS system administrators maintained it. Each page was developed by individual students and faculty while being supervised by the "Test Pilot" administrator at the university.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This project was completed and submitted in May of 2002. There have been no further amendments or modifications to the research study. There are no further subjects enrolled since completion of the study. Total number of participants was twenty. No adverse events occurred. The number of subjects enrolled to the study since last APR at WRAMC is 20 and the total enrolled to date at WRAMC is 20. The total number enrolled study-wide is 20, if multi-site study.

### CONCLUSIONS

Are providers asking patients specifically about alternative medications?

Seventy percent of providers surveyed occasionally ask about alternative medication use. Twenty percent always ask about this use. The data collected suggest that providers make an effort to find out about alternative medications, though not at all times. Female providers appear to ask more often than male. This study shows that there is a lack of history taking about the use of alternative medications. JACHO standards will soon require the assessment and evaluation of alternative medication use. This JACHO change represents a national organization recognizing the need for evaluation, thus reinforcing the need to gather these data. While the questionnaire used in this study was sent to providers at WRAMC, screening forms for the providers were being developed concurrently which will prompt providers to ask patient about the use of alternative medications.

Do providers feel it is important to ask patients whether they are taking alternative medications?

Providers in this study displayed a concern with the increased use of alternative medications, and the potential for adverse interactions these medications can have with prescription medications. Two thirds of providers disagreed that alternative medications have little benefit to patients, and 90% agreed there is some health benefit. While 70% of the providers did not consider alternative medications dangerous to patients, 95% believed that alternative medications could interact or cause complications with prescription drugs. Sixty-five percent agreed they were aware of possible drug interactions with some herbal medications and were informing their patients about them.

Work Unit # 02-75013 [*Continued*]

A major concern is raised by the data showing that 95% of providers felt that patients are not fully aware of drug interactions occurring with alternative medication use. The findings suggest that providers are willing to consider the use of alternative medication, know that some patients are using these therapies, and have a basis of understanding for educating patients about these therapies. Providers appear to know about alternative medications and yet many do not recommend this to patients. When providers were asked if they suggest alternative medications to their patients, 60% said “no, while 40% said they did. The providers were almost equally split when asked if patients’ health improved when they took alternative medications. Forty percent said “no”, and 45% said “yes”. Providers reveal a trend towards acceptance of alternative medications, and the future of complementary medicine may include alternative medications along with traditional therapies.

## DETAIL SUMMARY SHEET

TITLE: Do Culturally Acquired Behavior Norms Impact Workplace Communication?

KEYWORDS:

PRINCIPAL INVESTIGATOR: Nussbaum, George F. COL AN

ASSOCIATES:

DEPARTMENT: Nursing

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 5 March 2002

### STUDY OBJECTIVES:

1. To identify culturally acquired behavioral norms that impact workplace communication episodes
2. To explore the perceptions of culturally acquired normative behaviors by race, gender, and rank in a medical military environment
3. To explore the influence of expected military norms as alterations of individually acquired cultural norms

### TECHNICAL APPROACH

This study is following a qualitative research design using the grounded theory approach. One on one interviews are being conducted with participants. The interviews are audio taped and later transcribed for analysis of content.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 22 and the total enrolled to date at WRAMC is 22. The total number enrolled study-wide is 22. I expect to interview an additional 10 participants.

There have been no adverse events with this research.

### CONCLUSIONS

Analysis of data is ongoing. There are no findings to report until all of the participants have been interviewed.

## DETAIL SUMMARY SHEET

TITLE: A Study of The Safety and Feasibility of Telenursing for Remote Cardiac Rehabilitation

KEYWORDS: cardiac rehabilitation, telenursing

PRINCIPAL INVESTIGATOR: Patrician, Patricia A. LTC AN

ASSOCIATES: MAJ Joy A. Walker, LT Casie Lamp, AN

DEPARTMENT: Nursing  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 14 May 2002

### STUDY OBJECTIVE

To evaluate the feasibility and outcomes of a remote, home-based cardiac rehabilitation program for CABG patients. Feasibility will be assessed qualitatively by recording in a log equipment difficulties encountered throughout the study. The following patient outcomes of a historical control (usual care) group will be compared to those of a telecardiac rehabilitation group.

### TECHNICAL APPROACH

This study is a two-group repeated measures design comparing a usual care/historical control group to an intervention group. Because of the ethical issues surrounding randomization to treatment and control groups when we have already identified a gap in services for postoperative CABG patients, and in conjunction with the WRAMC Commander's recommendations, the research team chose not to use a randomized design. While preparations are being made for the telenursing initiative, we will enroll the first twenty consecutive CABG patients who meet our inclusion/exclusion criteria. This first group will serve as our "historical" control group and will receive usual care. They will, however, be asked to complete surveys to assess the outcome variables. These surveys will be administered to both the control and the intervention groups using the same administration schedule, with the exception of those instruments applicable only to the telenursing group.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The number of subjects enrolled to the study since last APR at WRAMC is 5 and the total enrolled to date at WRAMC is 5.

We are beginning to prepare for the intervention group. Thus far, we have selected the equipment we will use for the remote cardiac rehabilitation group, and we are preparing the documentation in terms of protocols for cardiac rehabilitation, as well as the scripts the nurse will use to assess the patients. The script templates and the cardiac rehabilitation protocols have received the approval of our cardiologist and our cardiothoracic surgeon colleagues. We are nearly ready to submit an IRB application for the intervention phase of the study.

Thus far, our survey response rate has been 100%. There have been no adverse events.

### CONCLUSIONS

No conclusions have been reached at this time.



## DETAIL SUMMARY SHEET

TITLE: Army Nursing Practice In Operations Other Than War

KEYWORDS: military nursing, competencies, nursing practice, readiness

PRINCIPAL INVESTIGATOR: Agazio, Janice, RN DoD

ASSOCIATES: COL Laura Brosch LTC(P), Beverly Cornett LTC(P), Karen Gausman LTC(P), Richard Ricciardi, Ms. Norma Flaherty, Ms. Rebecca Torrance

DEPARTMENT: Nursing  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 9 July 2002

### STUDY OBJECTIVE

To describe Army nursing practice in operations other than war. The research question guiding this study will be: What is the practice by Army Nurse Corps officers in operations other than war?

### TECHNICAL APPROACH

This study will be guided by the Army Nursing Practice conceptual model (Kennedy, Hill, Adams, & Jennings, 1996) and components of readiness as described by Reineck (1999). Army Nurse Corps officers, both active duty and reserve component, will be asked to participate in an interview using a focused interview guide. These nurses will have completed an OOTW deployment within the past three years. Those in the continental United States, outside the local area, or overseas will be contacted for an interview by phone. Those in the local area will take part in a face-to-face interview. Those in the Fort Bragg area will be invited to take part in a face-to-face interview over a three-day site visit. Consent forms will be mailed in advance and returned, signed and witnessed, prior to the telephone interviews. Additionally, verbal consent will be obtained on the tape-recording before beginning any formal interview questions. The maximum sample size would be dependent upon the need for more interviews based on emerging data and achieving theoretical saturation (Sandelowski, 1986). Demographic data will be summarized and presented using frequencies and descriptive statistics. Qualitative data analysis as described by Miles and Huberman (1994) will be used to simultaneously analyze and direct data collection to answer the research questions.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Since funding was awarded in July, the project has been approved by the IRBs at USU (primary) and WRAMC. The study coordinator at Womack was deployed so that the proposal has not yet been submitted at that facility. Data collection has not yet begun on the project. No participants have been recruited so there are no adverse events to report.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

### CONCLUSIONS

None at this time.

## DETAIL SUMMARY SHEET

TITLE: The Role of Mentoring in the Career Advancement of Hispanic Army Nurses

KEYWORDS:

PRINCIPAL INVESTIGATOR: Combs, Elmer W., LTC AN  
ASSOCIATES:

DEPARTMENT: Nursing  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 20 August 2002

### STUDY OBJECTIVE

The aim of this study is to achieve a greater understanding of the perceived personal, professional, career development, and socialization patterns of Hispanic nurses in the US Army. This information could lead to innovative patterns of career development and retention of this minority group in the future.

### TECHNICAL APPROACH

This is a two-part study. In Phase I, a demographic data form and the Alleman Mentoring Scales Questionnaire (AMSQ) was distributed to 110 Hispanic Army Nurse Corps officers at multiple sites to collect information about their mentoring experiences. The AMSQ consists of 100 Likert-type items that measure different types of mentoring behaviors. In Phase II, these same participants have the opportunity to volunteer for a follow-up face-to-face interview. Only those individuals indicating a desire to be interviewed will be contacted by the PI.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There is no new literature that impacts this study. Study-wide, 35 of 110 surveys have been returned. (Phase I.) Of these, 14 participants have volunteered for the interviews. (Phase II.) At WRAMC, 3 of 7 surveys have been returned, and two of these participants have volunteered for interviews. A total of 13 surveys were not distributed at WRAMC due to deployments. No interviews have been conducted at any site.

### CONCLUSIONS

Collection of data is on going. No findings yet.

## DETAIL SUMMARY SHEET

TITLE: Musculoskeletal Injury in AMEDD Soldiers

KEYWORDS:

PRINCIPAL INVESTIGATOR: Combs, Elmer W., LTC AN

ASSOCIATES:

DEPARTMENT: Nursing

STATUS: C

SERVICE:

INITIAL APPROVAL DATE: 10 September 2002

### STUDY OBJECTIVE

The purpose of this study was to describe the magnitude, nature, and physiological, psychosocial, and lifestyle factors associated with musculoskeletal injuries in AMEDD soldiers assigned to Walter Reed Army Medical Center (WRAMC), Washington DC.

### TECHNICAL APPROACH

This one-year descriptive-correlation study employed a cross-sectional design to survey AMEDD soldiers. Study questionnaires were distributed to individual's duty sections with a cover letter and a return addressed, stamped envelope. Three weeks later, a follow-up letter and a second copy of the questionnaire were distributed to the duty sections of those subjects who did not initially respond.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Data collection is complete. A total of 1868 questionnaires were distributed with 635 soldiers returning the questionnaires. There is no new literature available on this phenomenon. Originally, the study questionnaires were to be mailed to participants. However, the Medical Brigade refused to provide a list of home addresses for AMEDD soldiers. Consequently, questionnaires were distributed by hand. An amendment was submitted and approved by the WRAMC IRB for this change in protocol. There have been no adverse events and no participant has withdrawn from the study.

The number of subjects enrolled to the study since last APR at WRAMC is 635 and the total enrolled to date at WRAMC is 635.

### CONCLUSIONS

Of those responding, 52.9% reported sustaining at least one musculoskeletal injury in the past year. PI is currently awaiting a detailed final data analysis report from the statistician.

## DETAIL SUMMARY SHEET

TITLE: Gender Differences in Propofol Dosage During Regional Anesthesia

KEYWORDS: Propofol, Regional Anesthesia

PRINCIPAL INVESTIGATOR: Peverini, Anthony, MAJ AN

ASSOCIATES: Amegin, Kristin, CPT AN

DEPARTMENT: Nursing

STATUS: C

SERVICE:

INITIAL APPROVAL DATE: 24 September 2002

### STUDY OBJECTIVE

To examine gender differences in sedative dosages of propofol during regional anesthesia.

### TECHNICAL APPROACH

The subjects were pre-medicated with IV midazolam 0.02-0.03 mg/kg prior to being transported to the operating room. Baseline vital signs and BIS scores were taken on arrival to the operating room. Subjects received a fluid load of 500 cc of isotonic solution as well as IV fentanyl 0.75-1 mg/kg. A subarachnoid block was placed in accordance with standard of care. After assessment that the subarachnoid block was established, propofol dosing began. Propofol was titrated to achieve sedation as indicated by a BIS score of 60-80. When the surgical procedure was finished, the propofol infusion was stopped, and the time and total dose given was noted on the data collection tool.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Data collection is complete on a convenience sample of 34 military healthcare beneficiaries age 18 to 65 presenting for lower extremity surgery. Data analysis using ANCOVA demonstrated a statistically significant difference in the dosage of propofol required to attain and maintain sedation between men and women ( $p=0.002$  and  $p=0.19$ , respectively.) This is consistent with findings from Gan et al, 1999, in which the researchers found a gender difference in propofol dosage during general anesthesia.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 34.

### CONCLUSIONS

This study found that during regional anesthesia using propofol for sedation, women require more propofol than men. This was true both for dosages used to attain and maintain sedation.

Report Date: 5 February 2003

Work Unit # 02-81003  
(Same study as 02-81002)

## DETAIL SUMMARY SHEET

TITLE: Evaluation of Problem-Knowledge Couplers in the Military Health System

KEYWORDS:

PRINCIPAL INVESTIGATOR: Raney, Lance MAJ MC  
ASSOCIATES:

DEPARTMENT: Ireland Army Community Hospital  
SERVICE:

STATUS: C  
INITIAL APPROVAL DATE: 26 March 2002

### STUDY OBJECTIVE

To evaluate the impact of Problem-Knowledge Couplers on clinical quality, resource consumption, and patient and provider satisfaction. To evaluate Couplers, we conducted a patient randomized controlled trial at two military treatment facilities: Ireland Army Community Hospital, Fort Knox KY, and Mayport Naval Branch Medical Clinic, Mayport FL.

### TECHNICAL APPROACH

This is a patient level randomized, controlled trial with a concurrent observational group and historical control group. Patients with scheduled appointments to be cared for by a select group of providers at the two study sites were randomized into the intervention (Coupler) group or control (non-Coupler) group.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Nothing in the last year in literature has affected this study. Patient enrollment ended 20 December 2002. During the period January 2003-March 2003 we will complete the data abstraction and data cleaning. Thus, no study findings have been generated since the Interim Analysis Enrollment Report sent to Walter Reed Army Medical Center on 13 January 2003. All amendments and/or modifications were submitted as a revised addendum on 13 January 2003 and were approved by the WRAMC HUC on 28 January 2003. Subject enrollment to date:

Fort Knox: Study Patients 904  
External Control Patients 466  
Total 1370

Mayport: Study Patients 1002

Cumulative: Study Patients 1906  
External Control Patients 466  
Grand Total Enrolled 2371

There were no adverse events at Ireland Army Community Hospital or Mayport Naval Branch Medical Clinic. However, four subjects withdrew from the study (two from the study clinic and two from the external control clinic). All four withdrew because they were concerned with losing their medical records for data abstraction purposes.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 1370. The total number enrolled study-wide is 2371, if multi-site study.

### CONCLUSIONS

None.

## DETAIL SUMMARY SHEET

TITLE: Nursing's Retention of Trauma Resuscitation Skills

KEYWORDS:

PRINCIPAL INVESTIGATOR: Driscoll, Dennis M. LTC AN  
ASSOCIATES:

DEPARTMENT: Landstuhl Regional Medical Center  
SERVICE: Wurzburg USAMEDDAC

STATUS: O  
INITIAL APPROVAL DATE: 13 November 2001

STUDY OBJECTIVE: The purpose of this research is to evaluate the ability of nursing staff to perform resuscitative actions for traumatic injury and determine the length of time these skills are retained.

### TECHNICAL APPROACH:

The design for this project is a prospective quasi-experimental investigation with mixed, factorial design (time X training). Up to 197 individuals will be recruited from the nursing staff of the 67<sup>th</sup> Combat Support Hospital, 212<sup>th</sup> Mobile Army Surgical Hospital and Landstuhl Regional Medical Center located in the European theater to produce a sample of 171 individuals (57- Nurse Corps Officers, 57 - 91WM6's and 57 - 91W's). Head Nurses and Wardmasters will be contacted to establish times for the research staff to present the project to the staff of each nursing unit. Individuals who volunteer to participate will be contacted by a member of the research team to schedule an appointment for the evaluation and training. An assumption is made that these individuals will not undertake any preparatory training prior to the evaluation phase. Each individual will be ensured that this project is a research project, and the grading is not pass or fail. Additionally, the individual's performance will not be reported to the supervisory chain; therefore, results cannot be used in job performance evaluations. There have been no changes to the approved protocol.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE:

No new findings have been located in the recent literature. Due to unforeseen deployment of the principal investigator and difficulty getting equipment shipped outside the US, there has been a delay in starting the project. We are currently interviewing for the research staff and anticipate recruitment of subjects starting in November. To date there has been no research volunteers enrolled.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

### CONCLUSIONS

This project is just getting underway. PI anticipates initial enrollment to begin in November 2002.

## DETAIL SUMMARY SHEET

TITLE: Remote Armed Forces Tele-ocular Health – A Pilot Study

KEYWORDS:

PRINCIPAL INVESTIGATOR: Ramirez, Haby I., CPT MS

ASSOCIATES:

DEPARTMENT: Landstuhl Regional Medical Center

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 28 May 2002

### STUDY OBJECTIVE

May 2003 APR not required.

### TECHNICAL APPROACH

May 2003 APR not required.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Final DCI approval 21 days before end of fiscal year 2003.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Injury Control and Running Footwear

KEYWORDS:

PRINCIPAL INVESTIGATOR: MAJ (ret) Dr. Joseph Knapik, Sc. D.

ASSOCIATES:

DEPARTMENT: Aberdeen Proving Grounds

STATUS: T

SERVICE: Epidemiology and Disease Surveillance INITIAL APPROVAL DATE: 12 March 2002

### STUDY OBJECTIVE

Protocol terminated.

### TECHNICAL APPROACH

Protocol terminated.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Protocol terminated.

### CONCLUSIONS

Protocol terminated.



## DETAIL SUMMARY SHEET

**TITLE:** Evaluation of the Feasibility of Use of Personal Digital Assistants (PDAs) by US Army Healthcare Providers and User Needs Assessment

**KEYWORDS:** personal digital assistant, medical digital assistant, handheld computer, physicians, nurses, pharmacists, medics, medical informatics, clinical decision support

**PRINCIPAL INVESTIGATOR:** Poropatich, Ronald COL MC

**ASSOCIATES:** G.R. Sessions, Ph.D., D. Rodbard, M.D., S. Davies, Ph.D., and W. Brandes, D.O., M.P.H.

**DEPARTMENT:** Telemedicine Directorate

**STATUS:** O

**SERVICE:**

**INITIAL APPROVAL DATE:** 19 February 2002

### STUDY OBJECTIVE

This study is designed to a) evaluate feasibility use of personal digital assistants (PDAs) by health care providers, b) help identify user needs based on actual experience with the use of these devices, and c) identify factors that would be expected to result in improved design of PDA hardware and medical software applications that can improve utility and usability for physicians, nurses, medics, pharmacists, and/or other health care providers in US Army Medical Environments. The study has the goal of identifying problems with existing devices and software, and suggesting approaches to resolve these difficulties.

### TECHNICAL APPROACH

We have conducted a study of 84 physicians, nurses, nurse practitioners, pharmacists, and combat medics at DeWitt Army Community Hospital and Walter Reed Army Medical Center to assess clinical needs for the use of mobile handheld Medical Digital Assistants (MDAs). MDAs are defined as Personal Digital Assistants – PDAs – configured for clinical application, often with wireless connectivity. Participants completed an initial questionnaire, received “core” training in the use of an MDA configured with ten or more medical and fourteen Personal Information Management (PIM) applications, and more than a dozen “utility” applications. They attended two focus group sessions, recorded more than 500 observations regarding applications using a log book (database) application on the MDA, participated in a Delphi session at the close of the two month study in order to indicate their preferences for medical and PIM applications, and made recommendations about hardware, software, and systems issues. Study participants had a wide range experience with Personal Computers and PDAs. We employed specially developed software to monitor application usage that automatically recorded the date, time, and duration of each use of each application, thereby providing an unambiguous record of the popularity of applications and changes in patterns of usage with time.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

We encountered several barriers to implementation of the devices and devised methods to respond to those challenges. We have addressed selected issues relating to usability of the device. More than 20,000 uses of the MDA were recorded. The most popular clinically oriented applications were ePoctrates (drug database – 13% of all uses), Harrison’s Textbook of Medicine and 5 Minute Clinical Consult (10%), and other reference materials, decision support tools, treatment guidelines, and medical calculators. The most popular PIM functions were Date Book (17%), Address Book (18%), To Do List, Memo Pad, and Calculator. There were minor but systematic differences in the patterns of use by the several categories of health care providers. Usage was highest initially as participants became familiar with the devices, and then declined to a modest, steady state level. Participants gained sufficient information to be able to make informed recommendations at the time of the Delphi Session. Rankings obtained at the Delphi sessions at the close of the study corresponded closely to the actual level of usage throughout the study. There were strong recommendations from the participants that 1) the MDA be integrated with the available hospital systems (e.g. CHCS), 2) individual participants be able to download and install software and configure the devices to meet their own needs, 3) additional resources be devoted to improving the accuracy and

reliability of the medical decision support applications, integration and linking of medical applications, and aids to improve ease of learning, use, and navigation. Review of recent literature yielded 26 references. Adverse Events: None. Number of subjects enrolled: 84 (49 at WRAMC, and 35 at DACH). Subjects withdrawn: None.

The number of subjects enrolled to the study since last APR at WRAMC is 49 and the total enrolled to date at WRAMC is 49. The total number enrolled study-wide is 84, if multi-site study.

### CONCLUSIONS

The research team observed the needs for 1) expanded training (with courses, tutorial, and demonstration software), 2) “help-desk” support for use of both the hardware and the software, 3) automated approaches to software installation and maintenance, 4) internet connectivity for email and World Wide Web, 5) data encryption, and 6) access to medical records. Most importantly, the MDA, like any piece of technology, must be introduced with careful attention to existing workflow processes and combined with clinical process re-engineering to take advantage of the mobile and (optionally) wireless functions. There were requests for increased standardization of applications, to provide a single “system” rather than a myriad of disconnected stand-alone applications. Similarly, there were requests for a high degree of customization to meet the needs of each category of healthcare provider, each medical or clinical subspecialty, each institution, and ultimately each provider. Relatively minor issues created the majority of the problems encountered (e.g. batter failure and replacement, loss of styluses, and installation of software for HotSync’ing on individual PCs). The US Army Medical Department must make important policy decisions regarding use of wireless communication, access to identifiable patient data, data security standards, future integration with CHCS-II and other enterprise-wide information systems, and use of MDAs on a “personalized” or institutionalized basis. Large-scale implementation will require extensive training and ongoing support from Information Management professionals. Selection, standardization, testing, and integration of software will require significant resources. In view of the rapidly evolving hardware, software applications, and level of sophistication of US Army personnel, all of these systems will need to be tested extensively for usability on an interactive basis to optimize human factors, ergonomics, and the person-machine interface, both pre- and post-implementation.

## DETAIL SUMMARY SHEET

TITLE: Benchmark Usability Study of Medical Digital Assistants, Participatory Design, and Visioning

KEYWORDS: personal digital assistant, medical digital assistant, handheld computer, usability, ease-of-use, accuracy, efficiency, effectiveness, user-friendliness, physicians, nurses, pharmacists, medics, medical informatics, clinical decision support

PRINCIPAL INVESTIGATOR: Poropatich, Ronald COL MC

ASSOCIATES: G.R. Sessions, Ph.D., M. Wiklund, D. Rodbard, M.D., Eric Smith, Brian Lyons, M. Keeney, Ph.D.

DEPARTMENT: Telemedicine Directorate  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 16 April 2002

### STUDY OBJECTIVE

This study is designed to identify factors to improve design of Personal Digital Assistant (PDA) hardware and software applications that will result in improved usability for physicians, nurses, medics, pharmacists and other health care providers in U. S. Army medical environments. Additionally the study will identify problems with existing devices and software and develop approaches to resolve these difficulties. [Note: when a PDA is used primarily for medical applications in a healthcare environment, we shall utilize the term "Medical Digital Assistant" or "MDA".]

### TECHNICAL APPROACH

We expect to recruit up to forty participants from among health care providers assigned to Walter Reed Army Medical Center (WRAMC), Washington, DC and DeWitt Army Community Hospital, Ft. Belvoir, VA. Participants will be scheduled for individual laboratory sessions lasting no longer than three hours. To minimize the burden on participants, the laboratory sessions are conducted in a suitable room that is as close as possible to their normal work location, using a portable laboratory equipment kit. Participants perform a series of tasks that require the health care provider to interact with a PDA computer while we observe and make hand-written notes and video and audio-recordings of their behavior for later analysis. Each task should require no longer than 15 minutes to complete. At the end of the laboratory session, the participant is de-briefed, thanked for their participation, and invited to participate in a later session for participatory design and envisioning of potential applications of PDAs in the future. During the participatory design and envisioning session, participants provide suggestions to create a proposed new design.

### PRIOR AND CURRENT PROGRESS

We have conducted phase I of related studies, "*Evaluation of the Feasibility of Use of Personal Digital Assistants (PDAs) by U.S. Army Healthcare Providers and User Needs Assessment*," under a separate protocol to identify the clinical needs and conduct a feasibility study of the use of PDAs by healthcare providers at WRAMC and at DeWitt Army Community Hospital. The planning for the usability studies has been completed. We now intend to focus on systems such as BMIST and related systems for recording of medical histories, physical examination, and medical/clinical progress notes. Preliminary observations regarding the usability of the PDAs/MDAs have been made in the context of the user needs assessment and feasibility study.

REVIEW OF RECENT LITERATURE

(Nothing in the recent literature indicates an increase or change or risks to participants. Nothing in the recent literature would suggest that the potential benefits or value of findings of the present study have been diminished relative to the time when the study protocol was approved.)

The 2002 Annual Symposium of the American Medical Informatics Association included several papers regarding the use of PDAs or MDAs by clinicians in a wide variety of settings. None of these studies replicated what we are doing in our current study.

Adverse Events: None

Subjects withdrawn: None

Number of subjects enrolled: None. Recruitment has been postponed pending completion of the study to determine the clinical needs of healthcare providers in the US Army healthcare environment.

CONCLUSIONS.

The results of the study are not yet available. We expect that the study will be completed within the next few months. We hereby request an extension of the approval by the CIC for the next year.

## DETAIL SUMMARY SHEET

TITLE: Neuromuscular Rehabilitation Via Telebiofeedback as a Portal for Home Care

KEYWORDS: hemiplegia, gait, telebiofeedback, neuromuscular rehabilitation, telemedicine

PRINCIPAL INVESTIGATOR: LTC Raul Marin MC

ASSOCIATES: Tamara Cyhan, BSN, RN; CPT Susan Davis, MPT; Russell Henderson P.O.; Robin Howard, Ph.D.; LCDR Janet Keais, D.O., MS; Barri Miller, MPT; CPT Charles Quick, OT; Jill Schuyler, MS; CPT Matthew Walsworth, MPT; Joan Walter, P.A.-C

DEPARTMENT: Telemedicine Directorate  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 30 April 2002

### STUDY OBJECTIVE

The goal of this study is to determine the feasibility of rehabilitation for patients with chronic gait impairments following a central nervous system insult using an EMG biofeedback system conducted by a therapist remote from the patient location via "Tele" methodologies.

### TECHNICAL APPROACH

The technical approach involves the use of a patented EMG biofeedback technology (BioRehab Systems™) to conduct rehabilitation therapies on patients who have sustained specific neurologic injuries (i.e. hemiplegia). In addition, the therapies are conducted using Telemedicine technology from a base to a remote location.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The protocol was initiated on 24 October 2002. One subject has completed the study and one is currently receiving the biofeedback treatment. We submitted an addendum on 25 November 2002 regarding minor changes in the Data Collection Sheets, additions and subtractions of Associate Investigators, addition of a specific exclusion criteria, and submission of an advertisement for the study. These addenda were approved by DCI and are currently being implemented.

The number of subjects enrolled to the study since last APR at WRAMC is 2 and the total enrolled to date at WRAMC is 2

### CONCLUSIONS

Not applicable at this time. Data is still being collected.

## DETAIL SUMMARY SHEET

TITLE: A Randomized Clinical Trial of Cognitive-Behavioral Treatment for Post-Traumatic Stress Disorder in Women

KEYWORDS: Post-Traumatic Stress Disorder

PRINCIPAL INVESTIGATOR: Engel, Charles C. LTC MC  
ASSOCIATES:

DEPARTMENT: Deployment Health Clinical Center  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 16 October 2001

### STUDY OBJECTIVE

The objective of the study is to evaluate the efficacy of prolonged exposure therapy for treating PTSD and associated problems in active duty and veteran women. The work will significantly expand knowledge about the treatment of PTSD in military women.

### TECHNICAL APPROACH

The methodology for the study is summarized below:

All participants, including self-referrals, will enter the study through referrals by mental health clinicians. Following informed consent, participants will be screened for inclusion and exclusion criteria. If they meet these criteria and agree to participate, they will be randomly assigned to one of the two treatments, which will occur weekly for 10 weeks. Subjects will be assessed before treatment, immediately following treatment, and 3 and 6 months after the end of treatment.

- (Initial entry into Mental Health program for self-referrals)
- Screening phase 1: Referral source questioned regarding inclusion and exclusion criteria
- Screening phase 2: First meeting with potential subject to gather information about demographic background, explain the study protocol, and ascertain willingness to enter the study
- Screening phase 3: Subject gives informed consent and is interviewed to establish inclusion and exclusion diagnoses; baseline assessment performed if subject is eligible and agrees to participate
- Randomization assigned
- Scheduling of initial session with therapist
- Treatment begins
- Treatment ends
- Post-treatment assessment
- Interim assessment (3 months)
- Final assessment (6 months)

\*Enrollment will take approximately three weeks

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no study findings, yet, as the research has just begun. There have been a few amendments/modifications to the recruitment material. This is the study's first annual review. There is currently one patient enrolled in the study. The study's total enrollment, since its approval date is two. However, one patient was withdrawn from the study due to a serious adverse event. There have been no other adverse events at Walter Reed. Below is an account of information relating to the entire multi-center study, and includes data from all sites. There have been four severe adverse events study-wide. A brief synopsis of these events is provided below:

Work Unit # 02-89003 [*Continued*]

1. Walter Reed Army Medical Center, site 201, patient was hospitalized for intense anger, anxiety, and violent thinking. Symptoms seemed to be a result of intense work issues relating to her angry outbursts or flashbacks at work related to PTSD. The patient was admitted to the hospital 7/15/02, and discharged on 7/26/02.
2. Portland, site 648, patient spend 4 hours in the ER for suicidal ideation.
3. Portland, site 648, patient was hospitalized for dissociation and the patient was released 4/12/02.
4. Dallas, site 549, patient attempted suicide and was hospitalized after having an argument between her father and her fiancée.

Patients that have withdrawn from the entire study, (all sites): 32 patients have withdrawn from the study. The reasons for withdrawal breakdown as follows:

- 4 logistics, childcare
- 1 suicidal, homicidal ideation
- 3 disliked treatment
- 21 had other reasons
- 1 was lost to follow up

The number of subjects enrolled to the study since last APR at WRAMC is 3 and the total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 93, if multi-site study.

CONCLUSIONS

No conclusions are available at this time.

## DETAIL SUMMARY SHEET

TITLE: Veterans' Status, Health, and Mortality in Older Americans

KEYWORDS: Survival Analysis, Mortality Differentials, Health Status

PRINCIPAL INVESTIGATOR: Liu, Xian Ph.D. DoD

ASSOCIATES: Charles C. Engel, Jr. MD, Han Kang, Ph.D.

DEPARTMENT: Deployment Health Clinical Center

STATUS: O

SERVICE:

INITIAL APPROVAL DATE: 22 January 2002

STUDY OBJECTIVE

1. To describe the distribution of older Americans by veteran status, the associations of such a distribution with various measures of health status (chronic disease, mental disorder, disability, subjective assessment), and the connection of these associations with the level of old-age mortality and its causes.
2. To develop a series of survival models to test the underlying hypothesis that at older ages veterans tend to have higher mortality than do their non-veteran counterparts, both generally and by different causes of death, mainly by means of physical illnesses and mental disorders. This negative impact tends to get stronger as a cohort age. These models will be examined both in the presence and in the absence of different dimensions of health conditions. It is intended to determine the extent to which each health component, physical or mental, will transmit the effect of veteran status on the cause-specific risk of dying in later life.
3. To particularly test the hypothesis that mental health plays an equally important, if not more important, role as does physical health in veterans' excess mortality at older ages, both generally and cause-specific. This analysis will adjust for the confounding effects of socioeconomic and demographic characteristics.
4. To estimate a set of structural survival models that will further test the aforementioned hypotheses within an integrated framework. The structural models will together describe the process of how veteran status affects the mortality of older Americans by means of physical health, mental disorders, and some unidentified factors while controlling for the confounding effects of other related factors. Because the analysis involves different causes of death (e.g. internal or external), a competing risk framework will be specified.

TECHNICAL APPROACH

Cross-Sectional Data Analysis: The PI will seek to model veteran status, represented by several status- and era-specific categories, in relation to serious illness, chronic disease, disability, self-rated health, CES-D scale, and cognitive impairment. The purpose of this preliminary analysis is to estimate and test linkages between veteran status and the endogenous variables for ascertaining the existence of intervening influences of health status on the association of veteran status with cause-specific mortality at older ages. Specific statistical techniques will be used according to the nature of the dependent variable. For example, in the context of self-rated health, the PI will employ the ordered probit model to assess the impact of veteran status on subjective physical health adjusting for a number of control variables such as age, gender, education, ethnicity, and social relationships. The application of this approach will be based on the assumption that there exists a normally distributed latent factor indicating general health, and that self-rated health is the discrete realization of this factor. The PI will determine whether the two clusters of health conditions, physical and mental, will be better reflected in composite factors or by defining multiple measures for each health dimension. He will construct a number of endogenous factors representing "health conditions" for estimating and testing the structural model on veteran status and the mortality of older Americans.

One-Equation Survival Analysis: The PI will apply a set of one-equation hazard rate models to explore whether veterans have an elevated mortality at older ages versus non-veterans. He will define a Weibull distribution of the hazard function to model the survival rate of older Americans, as associated with an individual's veteran status and some other variables. This specification is based on the observation that among older persons, mortality generally goes up with age. The PI considers the application of the Weibull mortality function most appropriate for the description of mortality processes within a limited time interval, as evidenced by previous research.



Independent variables in the analysis will include veteran status, serious physical conditions, chronic physical conditions, functional status, self-rated health, CES-D score, cognitive impairment, and the aforementioned control variables. A series of one-equation survival models will be performed to assess whether the relationship between veteran status and old-age mortality holds in the presence or absence of physical health conditions and mental disorders. Three sets of one-equation hazard rate models will be constructed: General mortality model, mortality model of internal causes, and mortality model of external causes.

Structural Survival Analysis: As a last step, the PI will define a set of structural hazard rate models to estimate and test the positive effect of veteran status on the mortality of older Americans and its pathways, using the statistical perspective he has developed (Liu, 2000). In particular, he will specify both a full model and a set of sequential reduced-form equations on the basis of findings derived from the analyses described in the paragraphs above. Whereas the full model estimates only the direct effect of veteran status on the mortality, the final reduced-form equation will measure their total effects. By eliminating endogenous variables in sequence from the full model, the indirect influences of the veteran status by means of a given cluster of health status variables can be estimated and tested. Specifically, the PI will calculate the indirect effect of veteran status on the mortality of older Americans by means of physical illness alone, mental disorder alone, and physical and mental health jointly. In the estimation process of this structural model, the PI will recognize and estimate the prediction biases incurred by eliminating endogenous variables, and derive an adjustment factor for each reduced-form model. As a result, the direct, the total, and the indirect effects of veteran status will be estimated and statistically tested adjusting for an older person's demographics, socioeconomic status, and social relationships. Three sets of structural hazard rate models will be constructed for, respectively, general mortality, mortality from internal causes, and mortality from external causes. (No modifications so far.)

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The PI has been working on a manuscript on the effect of veteran status on the mortality of older Americans, co-authored with the two consultants of the proposed research, Dr. Charles C. Engel, Dr. Han Kang, and Dr. David Cowan. The major findings are stated in the "Conclusions" section below. Additionally, the PI submitted an abstract based on the findings to the 2003 Population Association of America (PAA) Annual Meetings, with an attempt to present this work to the PI's peers. As a part of the project, the PI is also working on an R01 grant proposal on the same topic that will be submitted to the National Institutes of Health by February 2003.

#### CONCLUSIONS

The PI and his co-authors have examined the excess mortality among American veterans age 70 years or older during a 2-3 year interval from 1993-1994 to the end of 1995. Data used for this study come from the Survey of Asset and Health Dynamics Among the Oldest Old (AHEAD). The research decomposes the effect of veteran status (veterans versus non-veterans) into the direct effect and the indirect effects by means of physical health conditions and mental disorders on the mortality of older Americans, using a structural hazard rate model. We have shown that at age 70 an older veteran is expected to have a slightly higher death rate than his or her non-veteran counterpart, and such an excess mortality among veterans tends to increase considerably over age, adjusting for an older person's socio-demographic characteristics. The direct and indirect effects of veteran status mostly perform in opposite directions, and such effects vary enormously in magnitude and direction over veterans shortly before age 70; after this crossover, veterans' excess mortality is increasing with age. Much of the mechanisms inherent in the excess mortality among older veterans are not captured by variations in their health status, especially among the Oldest-Old.

## DETAIL SUMMARY SHEET

**TITLE:** Use of Focus Groups to Develop Background Information In Support of Health-e VOICE – A Web-based Clinical Risk Communication Distance Learning Tool

**KEYWORDS:** focus groups, clinical risk communication, distance learning, deployment health, medically unexplained symptoms (MUS), qualitative analysis, primary care

**PRINCIPAL INVESTIGATOR:** Engel, Charles LTC MC

**ASSOCIATES:** Lt Col Joyce A. Adkins, USAF, BSC

**DEPARTMENT:** Deployment Health Clinical Center

**STATUS:** O

**SERVICE:**

**INITIAL APPROVAL DATE:** 12 February 2002

### STUDY OBJECTIVE

This protocol specifically and solely addresses the use of focus groups in support of developing Health-e VOICE, an interactive, web-based learning tool for improving Department of Defense healthcare providers' capacity to facilitate provider and military personnel communication regarding deployment-related health concerns. The objective is to describe and construct providers', patients', and spouses' mental models (knowledge base, misconceptions, and beliefs) pertaining to deployment-related health concerns and medically unexplained symptoms (MUS) by conducting a series of focus groups. The focus group content will be used to identify key health messages, audience sensitivities, challenges, and barriers to effective clinical risk communication about deployment-related concerns and MUS. This information will help identify challenges and solidify ideas surrounding important online and content features of the Health-e VOICE tool.

### TECHNICAL APPROACH

Each focus group will take approximately three hours. The agenda will proceed approximately as follows: a member of the investigative group will describe the Post-Deployment Clinical Practice Guidelines (PD-CPG), describe the perceived need for improved clinical risk communication, and then briefly summarize the intent to develop and evaluate an online clinical risk communication distance-learning tool for providers. This will take approximately fifteen minutes, followed by a fifteen-minute question and answer period moderated by the investigator. After a short break, a focus group facilitator will lead the group for the remainder of the time in discussions of various topics arranged in a semi-structured interview format that will be devised prior to the first planning conference. The format will be organized and committed to paper such that a given line of questions will begin open-ended. If discussion wanes early, specific prompts will be used to foster further discussion on the topic of the initial question. Topics addressed in the semi-structured interview for focus groups attended by primary health care providers will include:

- General post-deployment health issues
- Nature and etiology of deployment-related health concerns
- Nature and etiology of medical unexplained symptoms
- Challenges to the primary care of deployment-related health concerns and MUSs
- What individuals and parties bear the personal and health care system burden, blame, and responsibility for concerns and symptoms
- Primary care barriers to communication around risks, concerns, and symptoms
- Appropriate management of concerns and symptoms
- Prognosis of deployment-related concerns and symptoms
- Anticipated opportunities, strengths, weaknesses, and challenges for the proposed Health-e VOICE tool
- Ideas and suggestions for future emphasis of the planned tool

Since the Health-e VOICE tool will be entirely web based, it will be desirable to determine MTF Internet accessibility, browser capability, patterns of Internet usage, and the extent of computer literacy among DoD healthcare providers.

To achieve this, a questionnaire will be distributed upon completion of the focus group. The questionnaire will be anonymous, take approximately five minutes, and will be restricted to primary healthcare providers only.

Discussion topics for focus group attended by both previously deployed military personnel and their spouses and non-previously deployed military personnel and their spouses will include:

- General post-deployment health issues
- Nature and etiology of deployment-related health concerns
- Nature and etiology of MUSs
- Personal experience with the DoD healthcare system
- Personal satisfaction with DoD primary healthcare providers in general, and their skill in communicating deployment-related concerns and risks in particular
- Anticipated opportunities, strengths, weaknesses, and challenges for the planned Health-e VOICE tool
- Ideas and suggestions for future emphasis of the planned tool

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

The study is not expected to commence until mid-February 2003, and, as such, study data has not yet been collected.

On November 5, an addendum was submitted requesting that the composition of focus groups containing service members be changed from a health status basis (“ill” and “healthy”) to a deployment status basis (previously and not previously deployed). As a consequence of this proposed reconfiguration, the originally approved focus group consisting of spouses of “ill” deployed service members would be deleted. Spousal input would be preserved as originally intended, with such individuals being invited to attend and participate, accompanied by their spouse. In addition, due to anticipated low numbers of available care providers at each of the five sites, we requested to combine the physician and non-physician primary care providers’ focus groups. As a result of these proposed changes, the number of focus groups would be three with the maximum number of participants at each site being 36, and the total for all five sites being 180. The addendum was reviewed and subsequently approved on November 26.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0. The total number enrolled study-wide is 0, if multi-site study.

#### CONCLUSIONS

Not applicable. The study is not expected to commence until February 2003.

## DETAIL SUMMARY SHEET

TITLE: Cognitive-Behavioral Intervention For Victims of Mass Violence (Project DE-STRESS)

KEYWORDS: PTSD, trauma, cognitive-behavioral treatment

PRINCIPAL INVESTIGATOR: Engel, Charles C., LTC MC

DEPARTMENT: Deployment Health Clinical Center  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 25 June 2002

### STUDY OBJECTIVE

To evaluate an abbreviated form of Stress Inoculation Training (SIT), a component of Cognitive Behavioral Treatment (CBT), which aims to provide effective self/stress management skills to individuals with Post Traumatic Stress Disorder (PTSD). The rationale behind this intervention is that with appropriate and intensive therapist input during a single session of therapy, supplemented systematically with self-paced and self-directed homework, promoted, prompted, and monitored via a specialized web-site, augmented by therapist feedback, and guidance delivered via the web, primary care patients with PTSD stemming from military trauma or mass violence can benefit from the strategies that have demonstrated efficacy in reducing PTSD symptoms.

### TECHNICAL APPROACH

The present study is a randomized control trial comparing the effectiveness of SIT, a well researched psychological treatment for PTSD, to that of the non-specific standard care (SC) provided in primary care settings on individuals experiencing PTSD symptomatology. This pilot study was initially designed to test his mode of treatment as an early intervention with victims of the Pentagon Attack. However, due to low recruitment rates and the fact that the events of September 11<sup>th</sup> took place over eighteen months ago, we have expanded the scope of the study to include individuals experiencing PTSD symptoms as a result of any military related trauma in the last two years. Doing this should not affect the internal validity of the study. We will still treat all the study participants in a primary care setting, using identical methods.

Potential participants who contact us are screened for PTSD by telephone based on the following criteria:

1. DoD Healthcare beneficiary
2. 18 years old
3. Experienced a military-related trauma
4. Experiencing PTSD symptoms

Consented participants complete a two-hour face-to-face interview after which they are randomly assigned to either the SIT or SC condition. At this point a two-hour training session is arranged to teach participants how to use the website and introduce them to other techniques used during the active intervention. Once a participant is engaged in active treatment, there are five planned phone calls made by the trainers to check on the participants. Additionally, participants may contact their trainers by phone or email at any time. Since the participant recruitment of this two-year study was delayed, we changed the follow-up outcome assessment intervals from six months and one year to three and six months. This was necessary so that we could get two follow-up data points within the two-year funding interval. We still plan to conduct a one-year follow-up, using existing staff resources. We originally planned to recruit only from Army facilities local to the National Capital Region. We have since expanded our recruitment sites to include Fort Lee.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

During the initial start-up period, we developed the content for the September 11<sup>th</sup> web site, wrote training manuals for the SC and SIT conditions, and generated a schematic of the web process and web variables. Once the subcontracts between Boston University (BU), the Henry M. Jackson Foundation, and Boston Web Design (BWD)

were secured, we worked very closely with the web design team to generate ideas and beta-test various web contents and processes. In the first week of November we had a fully functional web site.

We have submitted several addenda since the original protocol was approved.

Addendum One contained eight modifications:

1. We changed our PTSD measure from the Clinician-Administered PTSD Scale (CAPS) to the PTSD Symptoms Scale (PSS-I) in an effort to reduce participant burden during the assessment.
2. In order to answer several secondary hypotheses we added additional measures, including the Penn State Worry Questionnaire (PSWQ), SF-36, Social Support Questionnaire (SSQ), and Psychosocial Adjustment to Illness Scale (PAIS).
3. We also submitted a basic demographic questionnaire.
4. We changed our follow-up assessment from six and twelve months to three and six months.
5. We included several more recruitment sources, including the Behavioral Health and Sciences Departments, the Battalion Aid Station, the Army Service Group, the Pentagon Employee Assistance Program, and the Family Assistance Center.
6. Based on modification five, we sought permission to conduct assessments and training sessions at other military treatment facilities in the NCR. We initially proposed to assess everyone using space at the DiLorenzo Clinic. However, we decided that it would be more convenient for individuals to be assessed at the various Dewitt Healthcare facilities.
7. Although the original proposal had specified the hiring of two Ph.D. level psychologists, two well-qualified doctoral candidates in clinical psychology were hired for the positions.
8. Finally, some language changes were made to the original consent form. We changed "Supportive Counseling" to "Standard Care", "Therapy Session" and "Treatment Session" to "Training Visit, and "Therapist" to "Trainer". These changes were made after consultation with *Operation Solace* care managers who felt that the latter terms were less stigmatizing and more consistent with language used in a primary care setting.

We submitted Addendum Two in order to expand our recruiting sites to include Fort Lee. While we had originally planned to only recruit from the Washington DC area, it came to our attention that individuals from the 54<sup>th</sup> Quartermaster Company at Fort Lee had engaged in the rescue and recovery efforts following the attack on the Pentagon.

Addendum Three addressed a simple oversight in our original consent form. One of the principal investigators on the project has two affiliations...the National Center for PTSD at the Boston VA, and Boston University Medical School. WE had failed originally to include the Medical School on the original consent form, and addendum three corrected that oversight.

In Addendum Four we submitted our advertising materials for approval.

Addendum Five was submitted in order to expand our inclusion criteria. We had originally planned to focus on survivors of September 11<sup>th</sup>. However, due to funding timeline constraints and low recruitment rates, we have expanded our inclusion criteria to include any military-related trauma. We therefore recently completed a generic web site that can be used for any individual with a military-related trauma, which greatly expands the capability of our self-help format for research and applied contexts.

In March of 2003, we prepared a HIPAA authorization form that was approved by DCI in April of 2003. We will be utilizing this form for patients enrolling in the study after 15 April 2003.

We have completed 26 briefings in an effort to recruit participants and inform providers about our study. We have received 27 referrals. Of those 27, we have successfully contacted 21 potential participants and formally assessed 8. To date, we have enrolled 8 participants. To date, there have been no adverse events reported, and no data have been analyzed.

## CONCLUSIONS

This study is still in progress, and as such, no conclusions have yet been made.

## DETAIL SUMMARY SHEET

TITLE: Pentagon Post-Disaster Health Assessment

KEYWORDS:

PRINCIPAL INVESTIGATOR: Jacobs, Mark MA DoD

ASSOCIATES:

DEPARTMENT: Pentagon

SERVICE:

STATUS: O

INITIAL APPROVAL DATE: 4 October 2002

### STUDY OBJECTIVE

APR not required – non-research study.

### TECHNICAL APPROACH

APR not required – non-research study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

APR not required – non-research study.

### CONCLUSIONS

APR not required – non-research study.

## DETAIL SUMMARY SHEET

TITLE: A Multicenter Double-Blinded Study in Patients with Compensated Cirrhosis Due to Chronic Hepatitis C Who are Non-Responsive to Prior Interferon Alfa or Interferon Alfa + Ribavirin Therapy, Comparing Treatment with Thymosin Alpha 1 + Peginterferon Alfa-2a with Peginterferon Alfa-2a + Placebo

PRINCIPAL INVESTIGATOR: Sjogren, Maria, COL MC

DEPARTMENT: Clinical Investigation  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 23 October 2001

STUDY OBJECTIVE

The primary efficacy endpoints are:

- Proportion of patients who are HCV RNA negative from month 12 to month 18 (sustained virological response)
- Proportion of patients demonstrating an improvement in liver histology as measured by 2-point improvement of Knodell scores post treatment with no worsening in fibrosis score.

The secondary efficacy endpoints are:

- Proportion of patients with normal ALT at month 12 (end of treatment biochemical response)
- Proportion of patients with normal ALT at month 18 (sustained biochemical response)
- Proportion of patients who are HCV RNA negative at the end of treatment (end of treatment virological response)

TECHNICAL APPROACH

This is a multicenter, randomized, double-blinded study. A total of 500 patients will be included in the study, divided into two groups of 250 patients each. Twenty-five patients will be enrolled at this site. Treatment consists of Pegylated interferon alpha-2a 180 mcg SQ once weekly plus Thymosin alpha-1 1.6 SQ twice weekly compared to Pegylated interferon alpha-2a 180 mcg SQ once weekly plus placebo SQ twice weekly. Patients will receive treatment for 48 weeks and will be followed after the treatment period ends for an additional 24 weeks to ensure safety. Patients will be randomly assigned to one of these two groups by an interactive voice response system after stratification based on viral load, genotype, and type of previous therapy.

To be eligible for this study, participants must have detectable hepatitis C virus measured by qualitative PCR (Amplicor®), be over the age of 18, and have signed informed consent prior to the start of any study procedures. They must have been treated previously with a three-month or greater course of interferon monotherapy or interferon plus ribavirin and have not responded. "Non-responders" are defined as those patients who had detectable HCV RNA at any time point between four weeks prior to and two weeks after the end of therapy. They must have evidence of elevated ALT within twelve months prior to screening visit. They must have a liver biopsy within 12 months of study entry consistent with cirrhosis due to chronic hepatitis C as measured by METAVIR fibrosis score of 3 to 4. Eight unstained slides from this biopsy must be available for blinded premeasured by prothrombin time no greater than 3 seconds over normal, total bilirubin < 2 mg/dl, and no history of hepatic encephalopathy, bleeding varices, or ascites. An ultrasound of the liver within three months of study entry must be negative for hepatocellular carcinoma. The patient must be hemodynamically stable with normal TSH and adequate renal function. If female, she must be surgically sterile, post-menopausal, or willing to use a definitive method of birth control for the duration of treatment and for six months following treatment. Patients will be excluded from this study if they have:

- Used systemic corticosteroids within six months of entry
- Drug-Induced liver injury or evidence of any other liver disease
- Decompensated liver disease
- Concomitant or prior history of malignancy
- Active infectious processes that are not self limiting

- Autoimmune disease
- Previously been treated with pegylated interferon or Thymosin alpha 1
- Uncontrolled seizure disorder
- Had a liver transplant
- Abuse alcohol or IV drugs in the past year or used methadone
- Been determined by the investigator as being a poor medical risk or compliance risk
- Are pregnant

#### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

This study enrolled its first patient in April 2002 and there are no scientific findings to report at this point. A review of the recent literature reveals no new findings that may influence the conduct of this study.

The number of subjects enrolled to the study since last APR at WRAMC is 6. The total number enrolled at all sites is 40 as of 12 August 2002. Expected enrollment is 500 nationwide, with a total of 25 enrolled at WRAMC.

There have been no serious adverse events among enrolled subjects reported at WRAMC or at any other participating site, and no patients have withdrawn from this study to date. Of note, one patient experienced complications from his screening liver biopsy 24 May 2002. This was reported to WRAMC HUC as per policy. This patient fully recovered and subsequently enrolled in this trial. Adverse events that have been reported among the six subjects enrolled include: flu-like symptoms, fatigue, arthralgias, insomnia, headache, backache, abdominal cramping and diarrhea, dyspepsia, nausea, anorexia, weight loss, shortness of breath, decreased concentration, irritability, depression, increased nasal congestion, itching, rash, and decreased libido/decreased quality of erection. These side effects are well documented in the consent form. Infrequently reported adverse events that are not specifically mentioned in the consent form include: bad taste in mouth post injection, sensitive teeth, dry/sore eyes, cough, and graying of hair. All side effects reported have been classified as mild to moderate in severity, and have not required dose reductions or suspensions. They have been self-limiting or responded to symptomatic treatment in most cases.

Addenda to this study since its approval are as follows in reverse chronological order:

- 06 June 2002 – Submission of updated Zadaxin Investigator's Brochure
- 13 May 2002 – Patient diary and patient guide to reconstitution and self injection of Thymosin alpha-1 submitted to IRB (not available at time of original application)
- 09 April 2002 – 6<sup>th</sup> Pegasys Investigator's Brochure submitted for review
- 27 March 2002 – Associate investigator list updated and new 1572 generated
- 20 March 2002 – Addendum to specify dose of Thymosin alpha-1 as 1.6mg, inclusion criteria clarified, liver biopsy slide requirements for submission to central pathologist changed, Data Monitoring Committee review added, and minor administrative corrections
- 14 December 2001 – Approval to begin protocol work from HUC after submission of revisions
- 09 October 2001 – Approval with revisions by CIC and HUC 923 October 2001)

#### CONCLUSIONS

At the time of this writing, nine patients have been screened and six patients have been randomized to one of the two treatment groups. All patients are tolerating therapy with mild to moderate side effects that respond well to symptomatic treatment and time. Two patients have completed four months of treatment, two have completed two months of treatment, one has completed one month of treatment, and one patient just started therapy. Most common side effects are flu-like symptoms following Pegasys injections. No serious adverse events among enrolled patients have been reported. HCV results tested at month 3, 6, 9, and 12 are blinded so early efficacy data will not be available to report.



## DETAIL SUMMARY SHEET

**TITLE:** A Phase II, Double-Blind, Randomized, Placebo-Controlled, Multicenter Study of the Safety and Anti-fibrotic Efficacy of Interferon Gamma-1b (IFN- $\gamma$  1b) in Patients with Severe Liver Fibrosis or Compensated Cirrhosis Due to Hepatitis C

**KEYWORDS:** Interferon Gamma-1b, Fibrosis, Cirrhosis, Hepatitis C

**PRINCIPAL INVESTIGATOR:** Sjogren, Maria H. COL MC

**ASSOCIATES:** Kent C. Holtzmuller, Julia C. Friend, LeTony Holcombe

**DEPARTMENT:** Internal Medicine

**STATUS:** O

**SERVICE:** Gastroenterology

**INITIAL APPROVAL DATE:** 20 November 2001

### STUDY OBJECTIVE

The primary objective of this study is to evaluate the proportion of patients showing a reduction of one or more points on the fibrosis staging score (using the METAVIR staging system) on liver biopsy following treatment with one of two dose levels of Gamma interferon-1b for 48 weeks compared to placebo recipient. A secondary objective is to evaluate the safety and tolerability of IFN Gamma-1b (100ug or 200ug three times a week) administered subcutaneously for 48 weeks as assessed by clinical signs and symptoms and laboratory measures.

### TECHNICAL APPROACH

This is a double-blind, randomized, placebo-controlled, prospective multi center, three-arm study comprising 48 week treatment with one of two doses of Gamma Interferon or placebo administered thrice weekly, subcutaneously. Study participants are those who have met screening criteria based on medical history, physical exam laboratory tests, as well as having a required degree of fibrosis as determined by a pre-treatment liver biopsy. Patients are seen and evaluated throughout the study to monitor for any side effects. At the conclusion of the study, a follow-up liver biopsy will be done, as well as laboratory studies of stored serum for markers of liver fibrosis.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Patients withdrawn from study: None from WRAMC. Information not available for other sites.

Recent literature: none

Study findings: not available

Amendments: 2

Number of subjects enrolled at WRAMC: 09

AE for WRAMC site: hematuria and BPH (one subject)

AE for other sites: Serious AEs for subjects with liver disease receiving Gamma Interferon include Hepatic Encephalopathy, Fluid Overload, Diabetes Mellitus (non insulin requiring), Myocardial Infarction.

SAEs for subjects with Lung Disease receiving Gamma Interferon include Acute Renal failure, Decreased Pulmonary function, Lower Respiratory Infection, Dyspnea, Hypoxia, Respiratory Distress, Respiratory Failure, Viral Infection, Acute Renal Failure, Bacteremia/Urosepsis, Cholecystitis, Hemorrhage. All SAEs were reported to WRAMC HUC.

The number of subjects enrolled to the study since last APR at WRAMC is 9 and the total enrolled to date at WRAMC is 9. The total number enrolled study-wide is 322.

**CONCLUSIONS:** Nine subjects are currently enrolled and receiving study medication at the WRAMC site. To date, a total of 322 study subjects have been enrolled at various study sites throughout the United States. At WRAMC, there have been no dropouts to date and the study drug is well tolerated. No conclusions about the efficacy of the study drug can be made, as the study is ongoing.

## DETAIL SUMMARY SHEET

**TITLE:** A Multicenter Double-Blinded Study in Non-Cirrhotic Patients With Chronic Hepatitis C Who Are Non-Responders to Prior Interferon Alfa or Interferon Alfa + Peginterferon Alfa-2a With Peginterferon Alfa-2a + Placebo

**PRINCIPAL INVESTIGATOR:** Sjogren, Maria H. COL MC

**DEPARTMENT:** Clinical Investigation  
**SERVICE:**

**STATUS:** O  
**INITIAL APPROVAL DATE:** 26 March 2002

### STUDY OBJECTIVE

The purpose of this study is to determine the safety and effectiveness of treatment with Thymosin alpha-1 in combination with Pegylated interferon alpha-2a in adult patients with chronic hepatitis C already treated with and not responding to interferon monotherapy or interferon plus ribavirin combination therapy.

The primary efficacy endpoints are:

- Proportion of patients who are HCV RNA negative from month 12 to month 18 (sustained virological response)
- Proportion of patients demonstrating an improvement in liver histology as measured by 2-point improvement of Knodell scores post-treatment with no worsening in fibrosis score.

The secondary efficacy endpoints are:

- Proportion of patients with normal ALT at month 12 (end of treatment biochemical response)
- Proportion of patients with normal ALT at month 18 (sustained biochemical response)
- Proportion of patients who are HCV RNA negative at the end of treatment (end of treatment virological response)

### TECHNICAL APPROACH

This is a multicenter, randomized, double-blinded controlled trial. A total of 500 patients will be included in the study, divided into two groups of 250 patients each. Twenty-five patients will be enrolled at this site. Treatment consists of Pegylated interferon alpha-2a 180mcg SQ once weekly plus Thymosin alpha-1 1.6mg SQ twice weekly compared to Pegylated interferon alpha-2a 180mcg SQ once weekly plus placebo SQ twice weekly. Patients will receive treatment for 48 weeks and will be followed after the treatment period ends for an additional 24 weeks to ensure safety. Patients will be randomly assigned to one of these two groups by an interactive voice response system after stratification based on viral load, genotype, and type of previous therapy.

To be eligible for this study, patients must have detectable hepatitis C virus measured by qualitative PCR (Amplicor®), be over the age of 18, and have signed informed consent prior to the start of any study procedures. They must have been treated previously with a three-month or greater course of interferon monotherapy or interferon plus ribavirin and have not responded. "Non-responders" are defined as those patients who had detectable HCV RNA at any time point between four weeks prior to and two weeks after the end of therapy. They must have evidence of elevated ALT within twelve months prior to or including the screening visit. They must have a liver biopsy within twelve months of study entry with no evidence of cirrhosis as measured by METAVIR fibrosis score of 0 to 3. Eight unstained slides from this biopsy must be available for blinded pre and post treatment evaluation by the central pathologist. They must also have compensated liver disease measured by prothrombin time no greater than three seconds over normal, total bilirubin <2 mg/dl, and no history of hepatic encephalopathy, bleeding varices, or ascites. An ultrasound, CT scan, or MRI of the liver within three months of study entry must be negative for hepatocellular carcinoma. The patient must be hemodynamically stable with normal TSH and adequate renal function. If

Work Unit # 02-92009 [Continued]

female, she must be surgically sterile, post-menopausal, or willing to use a definitive method of birth control for the duration of treatment and for six months following treatment.

Patients will be excluded from this study if they have:

- Used systemic corticosteroids within six months of entry
- Drug-induced liver injury or evidence of any other liver disease
- Current or past diagnosis of cirrhosis
- Alpha-fetoprotein > 200ng/mL
- HIV infection
- Concomitant or prior history of malignancy other than cured skin or cervical cancers
- Decompensated liver disease
- Concomitant or prior history of malignancy
- Active infectious processes that are not self limiting
- Autoimmune disease
- Previously been treated with pegylated interferon or Thymosin alpha 1
- Uncontrolled seizure disorder
- Had a liver transplant
- Abused alcohol or IV drugs in the past year or used methadone
- Been determined by the investigator as being a poor medical risk or compliance risk
- Are Pregnant

The study is structured as follows:

Screening		Randomization	Treatment Phase (month)													Follow-Up (month)	
(Within 8 weeks before randomization)		Day 0	1	2	3	4	5	6	7	8	9	10	11	12	15	18	
Informed consent	X																
Medical history	X																
Physical exam	X		X		X			X			X			X	X	X	
Vital signs	X		X		X			X			X			X	X	X	
Abdominal ultrasound	X																
HCV RNA	X			X				X			X			X	X	X	
HCV genotype	X																
Stored serum*	X							X			X			X		X	
Pregnancy test	X																
Auto-antibodies	X							X			X			X		X	
Serum Ferritin	X																
TSH	X		X		X			X			X			X	X	X	
Chemistry	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Urinalysis	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Hematology	X	X	X	X	X	X	X	X		X		X		X	X	X	
ALT, AST	X	X	X	X	X	X	X	X		X		X		X	X	X	
Alkaline phosphates, total bilirubin	X	X	X	X	X	X	X	X		X		X		X	X	X	
Concomitant medications		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Adverse events		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
ECG	X													X		X	
Anti-HIV Ab	X																
Alpha-fetoprotein	X																
HbsAg	X																
Liver biopsy	X															X	

**PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE**

This study enrolled its first patient at WRAMC in August 2002 and there are no new scientific findings to report at this point. A review of the recent literature reveals no new findings that may influence the conduct of this study.

The total enrolled to date at WRAMC is 2. The total number enrolled study-wide is 213, as of this writing. Expected enrollment is 500 nationwide with a total of 25 enrolled at WRAMC.

There have been no serious adverse events among enrolled subjects reported at WRAMC and no patients have withdrawn from this study to date from this site. There was one serious adverse event at another site and one withdrawal both related to depression and mood changes. Adverse events that have been reported among the two subjects at WRAMC include: flu-like symptoms, fatigue, arthralgias, insomnia, heartburn, decreased concentration, irritability, dry skin, and neutropenia requiring dosage modifications of study medications and ultimately supportive therapy with Neupogen. These side effects are well documented in the consent form. All side effects reported have been classified as mild to moderate in severity. In most cases, they have been self-limiting or responded to symptomatic treatment.

Addenda to this study since its approval are as follows in reverse chronological order:

- 19 December 2002 – submission of protocol revision (extension of screening window, expansion of age inclusion criteria, clarification of ALT, TSH, and other inclusion criteria)
- 15 November 2002 – submission of 14 separate Pegasys IND AE reports on events that were observed in other clinical trials at other sites
- 17 October 2002 – submission of revision to protocol to inform IRB of establishment of independent data monitoring committee reviewing safety data generated by all sites involved with Thymosin alpha-1 studies
- 16 June 2002 – submission of updated Zadaxin Investigator's Brochure
- 14 May 2002 – received approval to begin protocol work from HUC
- 13 May 2002 – patient diary and patient guide to reconstitution and self-injection of Thymosin alpha-1 were submitted to IRB (not available at time of original application).
- 09 April 2002 – 6<sup>th</sup> Pegasys Investigator's Brochure submitted for review
- 20 March 2002 – Addendum to specify dose of Thymosin alpha-1 as 1.6mg, inclusion criteria classified, and liver biopsy slide requirements for submission to central pathologist changed. Data monitoring committee review added, and minor administrative corrections

**CONCLUSIONS**

At the time of this writing, five patients have been screened and two patients have been randomized to one of the two treatment groups. All patients are tolerating therapy with mild to moderate side effects that respond well to symptomatic treatment and time. One patient has completed four months of treatment, one patient just started therapy. Most common side effects are flu-like symptoms following Pegasys injections, one patient has required the initiation of Neupogen to support his neutrophil count enabling him to continue therapy. No serious adverse events among enrolled patients have been reported. HCV results tested at months 3, 6, 9, and 12 are blinded, so early efficacy data will not be available to report.

## DETAIL SUMMARY SHEET

**TITLE:** A Phase III Open Label Study to Evaluate the Safety and Efficacy of RU-8811 in Patients with Types 3 or 4 Non-Alcoholic Fatty Liver Disease (NAFL)

**KEYWORDS:** RU-8811, Steatosis, Non-Alcoholic Fatty Liver Disease

**PRINCIPAL INVESTIGATOR:** COL Maria H. Sjogren MC

**ASSOCIATES:** Kent C. Holtzmuller, Brian Mulhall, Julia Friend, Tony Holcombe, Alexandra Lindemann, Dale Cloyd, Inku Hwang, Marten Duncan, Kendell Mann

**DEPARTMENT:** Clinical Investigation  
**SERVICE:**

**STATUS:** O  
**INITIAL APPROVAL DATE:** 23 April 2002

### STUDY OBJECTIVE

The primary objective of this study is to evaluate changes in serum alanine transaminase (ALT) in patients with types 3 or 4 non-alcoholic fatty liver disease.

The secondary objectives are to evaluate:

- Changes in serum and plasma laboratory liver function markers including: aspartate transaminase (AST), gamma-glutamyl-transpeptidase (γ-GT), alkaline phosphatase (AP), lactate dehydrogenase (LDH), total bilirubin (TB), albumin (ALB), and protime (PT), triglycerides (TG), and total cholesterol (T-CHO).
- Changes in levels of the following plasma markers of fibrosis: procollagen III N peptide (PIIINP), hyaluronic acid (HA), and transforming growth factor B1 (TGF-B1).
- Changes in ultrasonography (US) pattern and radiologic severity of steatosis.
- Changes in Quality of Life as assessed by the Chronic Liver Disease Questionnaire (CLDQ).

### TECHNICAL APPROACH

This study is a Phase II, open label study of RU-8811 involving two centers (INOVA Fairfax and WRAMC) in patients with Types 3 or 4 NAFL. The study drug, RU-8811, will be given orally at a dose of 54 mcg (18 mcg TID) for 28 days. A total of twenty patients will be treated; at WRAMC the enrollment goal is ten patients. After the 28-day treatment period, there will be a 30-day follow-up period. A washout period (45 days) will be required for those individuals currently on medication for NAFL (Vitamin E and Ursodeoxycholic acid).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Recent literature: None. Study findings: Not available. Amendments: Three.

Adverse events for WRAMC site: Mildly distended abdomen (1 subject). Headache: (2 subjects). Abdominal Gas: (3 subjects). Diarrhea: (2 subjects). Nausea: (2 subjects). Malaise: (2 subjects). Chills: (1 subject). L eye inflammation: (1 subject). L ear erythema: (1 subject). Bowel incontinence: (1 subject). Musculoskeletal pain: (1 subject). As per the sponsor's request, the following labs were listed under AEs: GGT (elevations): (3 subjects). AST (elevations): (5 subjects). ALT (elevations): (5 subjects). Potassium (decreased level): (1 subject). Chol (elevations): (2 subjects). Glucose (elevations): (3 subjects). Trig (elevations): (2 subjects). Ldg (elevations): (1 subject). No SAEs have been observed to date.

Patients withdrawn from the study: WRAMC = 1. INOVA Fairfax = 1. The WRAMC patient withdrew because of job restraints. The number of subjects enrolled to the study since last APR at WRAMC is 1 and the total enrolled to date at WRAMC is 5. The total number enrolled study-wide is 12 if multi-site study.

### CONCLUSIONS

Five subjects have been enrolled to date. Four subjects have completed the treatment period. One subject is currently receiving study medication at the WRAMC site. To date, a total of twelve study subjects have been enrolled between the two sites. Study drug was tolerated well, without any serious adverse events noted. No conclusions about the efficacy of the study drug can be made to date because the study is ongoing.

Report Date: 1 October 2002

Work Unit # 02-92011

## DETAIL SUMMARY SHEET

TITLE: See Work Unit # 02-87004

KEYWORDS:

PRINCIPAL INVESTIGATOR:  
ASSOCIATES:

DEPARTMENT:  
SERVICE:

STATUS: N/A  
INITIAL APPROVAL DATE:

STUDY OBJECTIVE

TECHNICAL APPROACH

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

CONCLUSIONS

## DETAIL SUMMARY SHEET

**TITLE:** Combination of Ribavirin with Interferon Alfacon-1 or With Pegylated Interferon Alfa 2b as Initial Treatment For Difficult to Treat Subjects Chronically Infected With Hepatitis C Virus – Genotype 1

**KEYWORDS:** Hepatitis C, Genotype 1

**PRINCIPAL INVESTIGATOR:** Sjogren, Maria H., COL MC

**ASSOCIATES:** COL Kent Holtzmuller, MC, COL Milton Smith, MC, Amber Watts, M.A., Pia Casarino-Lepler, LPN, Marcos Amorim

**DEPARTMENT:** Clinical Investigation  
**SERVICE:**

**STATUS:** O  
**INITIAL APPROVAL DATE:** 25 June 2002

### STUDY OBJECTIVE:

To assess the sustained virologic response after 48 weeks of treatment with either 15 mcg interferon alfacon-1 (Infergen ®) three times a week (TIW) plus daily ribavirin (Ribavirin manufactured by Three Rivers Pharmaceuticals) or 1.5 mcg/kg of PEG interferon alfa-2b weekly plus daily ribavirin (Rebetol®) in previously untreated patients with chronic hepatitis C who are infected with HCV genotype 1.

### TECHNICAL APPROACH:

Patients who have not previously been treated will be screened for eligibility according to study criteria and enrolled if eligible. Once enrolled, patients will be randomly assigned to one of the two treatment groups and stratified according to their viral load (high or low). They will be seen at the clinic at baseline, week 1, week 4, and every four weeks (except week 44) for the duration of therapy (up to 48 weeks). They will also be seen in the clinic at 12 weeks and 24 weeks after the completion of therapy. During these clinic visits, they will have laboratory tests done and complete questionnaires according to the protocol. After 24 weeks of therapy, a test of the patient's HCV RNA viral load will be conducted. If the patient is HCV RNA positive, s/he will discontinue treatment and begin the follow up period. If the patient is HCV RNA negative s/he will continue on treatment for up to 24 more weeks and then proceed to the follow up period.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Enrollment in the study began on 16 January 2003. To date, 13 subjects have been enrolled study wide, and 4 at WRAMC. There is no recent literature or study findings to be reported at this time. One serious adverse event occurred at WRAMC and constitutes the only patient to be discontinued from the study thus far. The patient was hospitalized due to difficulty to arouse, increased fatigue and somnolence, and decreased concentration. No conclusive cause was found. The SAE was reported to HUC within 24 hours. Of the four subjects enrolled at WRAMC, the following expected adverse events were reported: 3 reported myalgia (2 mild, 1 moderate), 1 reported mild arthralgia, 1 reported mild inflammation at the site of injection, 2 reported insomnia (1 mild, 1 moderate), 1 reported mild fatigue (this does not include the patient with SAE), 1 reported mild headache, and 2 had depression (1 mild, 1 moderate). This is the first APR. The total number of subjects enrolled to date in the study at WRAMC is 4. The total number enrolled study-wide is 13.

### CONCLUSIONS

No conclusions can be made at this time.

## DETAIL SUMMARY SHEET

TITLE: The Effect of Platelet Rich Plasma on Postoperative Pain, Edema, and Ecchymosis in Cervicofacial Rhytidectomy – A Pilot Study

KEYWORDS:

PRINCIPAL INVESTIGATOR: Trebus, Daniel L., MAJ DC  
ASSOCIATES: Will, Michael J. COL DC, Haddad, Jihad LTC DC

DEPARTMENT: DENTAC  
SERVICE:

STATUS: O  
INITIAL APPROVAL DATE: 15 January 2002

### STUDY OBJECTIVE

To explore the effect of autologous platelet rich plasma (PRP) on postoperative pain, edema, and ecchymosis after application during facial cosmetic surgery procedures.

### TECHNICAL APPROACH

Patients will be scheduled for surgery prior to approaching them to participate in this study. Surgery dates for patients declining to participate will only be changed at the patient's request (to avoid the potential for appearance of coercion).

1. Informed consent obtained.
2. Standard preoperative assessment.
3. Experimental and control sides randomly assigned.
4. Surgical procedures performed on each side in identical fashion by same surgeons. PRP applied to one side just prior to closure of surgical wounds. Surgeons will not know which side receives PRP until the nurse tells them immediately prior to closure.
5. Follow-up appointments occur at set intervals for all patients according to normal protocol of independent evaluator (not in presence of the surgeons/investigators.)
6. Stopping rules – see protocol.
7. Data collected and analyzed as described in protocol.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

There have been no amendments to the research study since last review. The PI has changed. There have been no subjects enrolled since approval of protocol; therefore, there have been no study findings obtained thus far.

The number of subjects enrolled to the study since last APR at WRAMC is 0 and the total enrolled to date at WRAMC is 0.

### CONCLUSIONS

Although protocol is ongoing, no patients have been enrolled as of yet.



## DETAIL SUMMARY SHEET

TITLE: Comparison of Botulinum Toxin Injection for Plantar Fasciitis vs. Placebo - A Clinical Trial

KEYWORDS: Foot pain; Plantar Fasciitis; Botulinum toxin

PRINCIPAL INVESTIGATOR: Babcock, Mary Sabado CPT M

ASSOCIATES: Jabbari, Bahman COL MC; Foster, Leslie LTC MC

DEPARTMENT: Orthopaedics and Rehabilitation

STATUS: O

SERVICE: Physical Medicine & Rehabilitation

INITIAL APPROVAL DATE: 16 October 2001

### STUDY OBJECTIVE

The purpose of this study is to compare whether the pain response after injection of botulinum toxin differs from that of placebo in the treatment of plantar fasciitis after three weeks.

### TECHNICAL APPROACH

#### *Patient Selection*

Patients will be evaluated using the inclusion/exclusion criteria. Pregnancy will be ruled out by serum HCG level drawn at a laboratory facility.

#### *Group assignment and Randomization*

There will be two groups in this study. Group I will be the BTX-A group and Group II will be the Placebo group. Both groups will be blinded to the treatment they receive since the initial injection of BTX-A causes no unique sensation or paresthesia and cannot be distinguished from a saline injection. Since all patients included in this study have already failed a corticosteroid trial, this treatment will not be compared to the BTX-A injection. Subjects will then be randomized. Further group stratification according to age will not be conducted since identifying trends in age-related response is not in the study objective and will possibly require a larger population to achieve equivalent statistical power. However, since it will take several months to recruit up to 70 patients for this study, block randomization will be used in order to facilitate early analyses. The DCI Biometrics Section will provide randomization schedule. Only the Pharmacy and the clinical research nurse assigned to the Neurology service will be aware of group assignment and will prepare each syringe for administration (BTX-A and placebo). This role includes: (1) administering and reviewing the questionnaires with each subject, (2) preparing the syringes with either BTX-A solution or saline for each subject depending on their assigned group, and (3) filing patient records in a confidential and secured area. The physician and patient will be blinded as to which is the active and which is the placebo. At the end of the treatment, the patient and physician will be asked which treatment they believe was given.

#### *Pre-treatment evaluation*

Pain. Pain will be evaluated both subjectively and objectively.

1. *Pain VAS* – A visual analog scale to assess pain level will be used. Each subject will be asked to complete this scale, which consists of a 10cm-line with the ends labeled as “no pain” and “pain as bad as it could be.” Retest reliability with literate patients has been found to be 0.94 (6). Regarding validity, correlations between vertical and horizontal VAS were approximately 0.89 to 0.91 (5). This study will incorporate the horizontal scale.
2. *Pressure Algometry* – A pressure algometer will quantitatively assess muscle tenderness at the site of the plantar fascial insertion and at the other three muscles in the plantar fascia area to be considered for injection (quadratus plantae, flexor digitorum brevis and abductor hallucis). The device will be positioned perpendicular to the sole of the foot and incremental cutaneous pressures will be slowly applied over the described areas. The pressure in kilograms at which the subject first reports pain will be recorded. Three serial measurements will be taken and recorded. All correlations of within-experimenter reliability and between-experimenter reliability were highly significant ( $P < 0.01$ ).

3. *Maryland Foot Score (MFS)* – The MFS is also known as the Foot Function Form developed by the Painful Foot Center (PFC) at the University of Maryland. The MFS, administered by the physician, is based on a 100-point scale (0-100 with 100 being normal) which assesses foot pain and function in relation to pain, gait, stability, support, limp, motion and ability to climb stairs during pre-treatment and all post-treatment evaluations (14). This score is highly reproducible as it limits patient subjectivity by using specific questions. Based on the PFC scoring system, grading is as follows: excellent (90-100), good (75-89), fair (60-74) and poor (59 or less) (14). Though this tool is widely used in the orthopedic community, it has not been validated. However, it does provide a standardized way for physicians to record foot pain and function.

*Application of Treatment (Conducted during subsequent scheduled appointment.)*

BTX-A Group. The physician will inject 40u of BTX-A (1cc solution) just medial to the base of the plantar fascial insertion with special attention to be deep to the calcaneal fat pad. Additional injections of 15u BTX-A (1cc solution) will be administered into one of three other muscles (the most tender of the three per pressure algometry and patient verification) in the arch of the foot (Appendix C) quadratus plantae, flexor digitorum brevis, and abductor hallucis. Placebo Group. The physician will use the same procedure as outlined above except will inject 1cc of normal saline instead.

*Post-Treatment Evaluation*

The subject will return in three weeks for post-treatment evaluation. The subject will then be invited to return at intervals of two months, four months and six months for follow-up. During the post-treatment evaluation and each subsequent follow up visit, the patient will complete another Pain VAS (Appendix B2) and be reassessed by a medical practitioner who will obtain another MFS and pressure algometry measurements. In addition, the patient will also be asked to complete a Pain Relief VAS. According to Huskisson, since the initial and subsequent pain ratings tend to be correlated (coefficients of 0.62 and 0.63), a Pain Relief VAS is more advantageous than just comparing Pain VAS scores before and after treatment (11). In other words, despite their initial pain level, the patient has the same magnitude of potential response (18). An interim analysis will be conducted after the three-week visit. If there is statistically significant pain relief in the BTX-A group at that time, the study may be cut short and the treatment offered to the subjects in the placebo group. All patients will still be invited back during the scheduled follow up times and data will be collected to further assess duration of relief. If further treatment or specialty referral is indicated during this time, it will be recommended to the patient.

*Stopping rule*

If at any time during the study the patient decides to terminate the treatment sessions and seek other treatment strategies, the treating practitioner will support the patient's wishes and the principal investigator will be notified of the circumstances. The patient will be asked to contact the PI at the number listed on the cover page if the pain becomes worse after the treatment procedure. The PI will re-assess your involvement in the study and will make appropriate referrals and recommendations. If at any time early in the study, several patients report adverse effects or worsened pain, the study will be re-assessed and terminated if risks outweigh the proposed benefits. It is under these circumstances that the physician will be informed of which group the patient is in. The prevalence of adverse effects is minimal (less than 2%) and includes flu-like symptoms, allergic reaction, numbness and partial paralysis (3). Also, as with every injection, possible local infection can occur. This is minimized with clean preparatory technique just prior to the procedure. Patient dropout rate will be monitored.

Data Collection:

*Frequency*

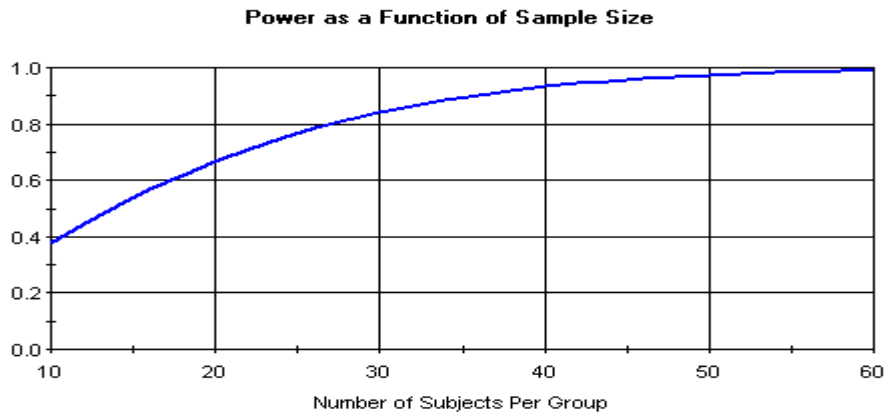
Data will be collected during the pre-treatment/initial evaluation, and post-treatment at three weeks, two months, four months and six months.

*Forms*

Three forms will be used: (1) to be completed by the patient on pre-treatment evaluation, (2) to be completed by the patient on post-treatment evaluation, and (3) to be completed by the provider on initial evaluation, treatment application, and post-treatment evaluation. Overall, the initial evaluation/post-treatment form will include subject demographics, duration of plantar fasciitis symptoms, previous treatments, and medication profile to include allergies. Furthermore, the treatment application form is simply a procedure note to include injection sites and

muscles injected as well as any complications. The primary outcome variable “relief of pain” will be assessed using the Pain Relief VAS post-treatment, the change in Pain VAS between pre-and post- treatment and increased tolerance on pressure algometry and improvement in the MFS before and after treatment. All measurements will be recorded before and after injection (either with BTX-A or placebo) except for the Pain Relief VAS, which will only be completed by the subject at each post-treatment evaluation. Post treatment Pain Relief VAS scores and Pain VAS score of 5 through 7 will be rated as “good” and VAS scores 7 or greater will be rated as “excellent”.

**Sample Size/Data Analysis:** In a previous study of treatment of myofascial low back pain using BTX-A, all patients in the treated group reported greater than 50% pain reduction (8). In the BTX-A injection treatment group, neither adverse effects nor worsening of pain or function occurred.



This sample size justification uses the study results from a previous protocol and professional experience. With a proposed sample size of 60 subjects (30 subjects in each group), the study will have 85% Power to yield a statistically significant result as shown in the above graph (SPSS Sample Power, 2.0. Chicago, IL, 2001). This computation assumes that the difference in proportions is 0.35 (specifically, the proportion indicating “good” and/or “excellent” relief for the treatment of plantar fasciitis is Grp1=0.50 versus Grp2=0.15) and a criterion of significance (alpha) set at 0.05. To account for dropouts and missing (or lost) data, up to 70 subjects (35 subjects in each group) should be sufficient as the total sample size for this study.

The primary outcome variable for the study is “relief of pain” as defined under DATA COLLECTION. Descriptive statistics will be reported for the study variables for the subjects in each study group. In order to address the study objective of comparing the proportion of subjects indicating “good and/or excellent” relief of pain between two groups, a Fisher’s Exact test will be used at each data collection period to evaluate the null hypothesis that the proportion of subjects in Grp1 indicating “good and/or excellent” pain relief is the same as the proportion of subjects in Grp2 indicating “good and/or excellent” pain relief. Additionally, to compare the median VAS scores between the two groups at each time period, a Mann-Whitney U test will be used to evaluate the null hypothesis that the median VAS score in Grp1 is not different from the median VAS score in Grp2. A paired T-test (or the nonparametric equivalent test) also will be used to ascertain whether the VAS scores are different within each group. As appropriate, multivariate analysis will also be performed to account for possible covariates or confounding variables identified during the analysis of data. All tests will be two-tailed and SPSS, v. 10 (Chicago, IL, 1999) will be statistical software package utilized for the analysis of study data.

#### **PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE**

Sixteen subjects enrolled. No adverse events noted thus far. No new literature regarding BTX and Plantar Fasciitis. The number of subjects enrolled to the study since last APR at WRAMC is N.A. and the total enrolled to date at WRAMC is 16.

**CONCLUSIONS** We will conduct an interim analysis when twenty subjects are recruited.

## DETAIL SUMMARY SHEET

**TITLE:** New Plantar Fasciitis Orthotic (PFOs) Versus Traditional Conservative Treatment for Plantar Fasciitis – A Novel Randomized Controlled Trial

**KEYWORDS:** plantar fasciitis, heel pain, orthotics

**PRINCIPAL INVESTIGATOR:** Hannah, Mary C., CPT SP

**ASSOCIATES:** CPT Christine R. Swiecki MC, CPT Michael Winters MC, CPT Cameron Stokes MC, CPT Evan Jones MC

**DEPARTMENT:** Orthopaedics and Rehabilitation

**STATUS:** O

**SERVICE:** Physical Medicine & Rehabilitation  
2002

**INITIAL APPROVAL DATE:** 6 August

### STUDY OBJECTIVE

To determine if there will be a difference between plantar fasciitis patients treated with Plantar Fasciitis Orthotics (PFO), relative rest, and ice and patients treated with standard of care treatment – viscoelastic heel pads, relative rest, and ice.

### TECHNICAL APPROACH

We will recruit up to 100 subjects with plantar heel pain from the four sites listed above and randomly assign each subject to one of two groups: PFO or viscoelastic heel pad. We will ask all subjects to wear their assigned shoe insert 100% of the time while weight bearing, to refrain from extra weight-bearing activities for one week, and to ice the painful heel for twenty minutes once a day for one week. The outcome measure is the already validated tool, Functional Foot Index. Subjects will complete the FFI questionnaire during their initial evaluation, at one week, at six weeks, and at six months. Thus, the study is a 2 (group) x 4 (time) repeated measures ANOVA. If a subject feels that the assigned treatment does not help decrease the heel pain or makes it worse, and he or she decides to drop out, the subject will be offered the opportunity to re-start with the other treatment. We will collect that data and analyze it separately.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Our original review of literature revealed that multiple studies have looked at multiple types of treatments for plantar fasciitis, and that no one particular treatment alone seems to work well for most patients except lithotripsy. I plan an updated review of the literature prior to the end of this year, which will be one year since beginning data collection.

We are in the data collection phase of the study and have not done any data analysis yet. Of the 24 subjects recruited at WRAMC and Kimbrough ACC, we have had five dropouts.

The number of subjects enrolled to the study since last APR at WRAMC is 14. The number enrolled at Kimbrough ACC is 10. Another 7 subjects have been recruited at Wilford Hall. None have been enrolled at William Beaumont. The total number enrolled study-wide is 31, if multi-site study.

### CONCLUSIONS

We have not drawn any conclusions yet because we are not in the data analysis phase of the study yet.

## DETAIL SUMMARY SHEET

TITLE: The Percent of Kidney Transplant Recipients Followed In a Single Center Outpatient Nephrology/Transplant Clinic With BK Virus Infection (WRAMC)

KEYWORDS:

PRINCIPAL INVESTIGATOR: Reynolds, Joel C., CPT MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Nephrology

STATUS: N  
INITIAL APPROVAL DATE: 11 February 2003

### STUDY OBJECTIVE

To determine the prevalence of BK virus infection in all consenting kidney transplant patients followed in the nephrology clinic at WRAMC and to identify possible associations between clinical and demographic data, and the likelihood of having the disease.

### TECHNICAL APPROACH

Up to 120 renal transplant recipients followed in the WRAMC Nephrology/Organ Transplant Service (OTS) clinic with functioning renal allografts will be studied.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: ARBITER III – Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol – A 1-Year Open Label Investigation On The Effects Of Long-Acting Niacin On Carotid Intimal Thickness

KEYWORDS:

PRINCIPAL INVESTIGATOR: Taylor, Allen J., LTC MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Cardiology

STATUS: N  
INITIAL APPROVAL DATE: 10 December 2002

### STUDY OBJECTIVE

To evaluate the effect of niacin when added to an HMG-CoA reductase inhibitor on carotid atherosclerosis progression.

### TECHNICAL APPROACH

This will be an open-label, observational drug study. ARBITER II subjects with known coronary vascular disease who had LDL cholesterol less than 130mg/dL and HDL cholesterol less than 45mg/dL while on statin therapy will be enrolled.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Pride Study – Protection During Saphenous Vein Graft Intervention to Prevent Distal Embolization

KEYWORDS:

PRINCIPAL INVESTIGATOR: Dixon, William, MAJ MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Cardiology

STATUS: W  
INITIAL APPROVAL DATE: 17 December 2002

### STUDY OBJECTIVE

Study withdrawn.

### TECHNICAL APPROACH

Study withdrawn.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn.

### CONCLUSIONS

Study withdrawn.

## DETAIL SUMMARY SHEET

TITLE: Proteomic Analysis of Coronary Artery Disease

KEYWORDS:

PRINCIPAL INVESTIGATOR: Elgin, Eric, CPT MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Cardiology

STATUS: N  
INITIAL APPROVAL DATE: 21 January 2003

### STUDY OBJECTIVE

The objective of this study is to define a proteomic spectral fingerprint for coronary artery disease. This is an extension of a previously approved addendum to WU #00-1201: Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol - A Randomized Trial Comparing the Effects of Atorvastatin and Pravastatin on Carotid Intima-Media Thickness. The addendum to WU #00-1201 outlined the parameters of the project to perform the training phase of the study. This protocol includes the parameters for the validation phase.

### TECHNICAL APPROACH

The study will have two phases, a training phase and a validation phase. The training phase will attempt to generate a spectral fingerprint for CAD from samples with clinical CAD. A training set of 50 samples from patients with clinical CAD will be compared to samples from patients with elevated LDL but no history of clinical CAD. The spectral fingerprint is generated using the SELDI-TOF technique described above. The results produce a spectral tracing of the mass/charge ratio plotted against the relative intensity of each peak. The second phase will validate the fingerprint with blinded samples from patients both with and without CAD. These samples will include patient samples from the ARBITER, ARBITER-II and PACC trials and will not include any samples that were used in the training phase of the study. The ARBITER and ARBITER-II samples will be used for the blinded samples of patients with clinically manifested CAD. The CAD samples from ARBITER include patients with a reported history of angina, prior myocardial infarction, or CABG. The ARBITER-II study included only patients with clinical CAD already on a statin with low HDL. The inclusion of patients from both the ARBITER (not on statin therapy) and ARBITER-II will provide a more diverse validation sample set. The non-CAD samples will be drawn from the PACC study and will include patients without prior history of clinical CAD. From PACC, two different populations will be studied.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: Organized Program to Initiate Life-Saving TreatMent In HospitaliZEd Patients with Heart Failure (OPTIMIZE-HF) – An Internet-Based Registry and Process of Care Improvement Program for Heart Failure Patients

KEYWORDS:

PRINCIPAL INVESTIGATOR: Welka, Stephen, MAJ MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Cardiology

STATUS: W  
INITIAL APPROVAL DATE: 4 February 2003

### STUDY OBJECTIVE

Study withdrawn.

### TECHNICAL APPROACH

Study withdrawn.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn.

### CONCLUSIONS

Study withdrawn.

## DETAIL SUMMARY SHEET

TITLE: A Prospective United States Investigation of the CARDIA STAR™ Patent Foramen Ovale Closure Device

KEYWORDS:

PRINCIPAL INVESTIGATOR: Simpson, Daniel MAJ MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Cardiology

STATUS: N  
INITIAL APPROVAL DATE: 25 March 2003

### STUDY OBJECTIVE

The primary objective of this clinical study is to demonstrate the safety, effectiveness, and clinical utility of the CARDIA STAR™ Patent Foramen Ovale Closure System. The following study objectives were identified to achieve this goal:

- To evaluate the safety of the CARDIA STAR™ Patent Foramen Ovale Closure System compared to anticoagulation therapy at 12 months
- To quantify the effectiveness of the CARDIA STAR™ Patent Foramen Ovale Closure System
- To evaluate the clinical utility of the CARDIA STAR™ Patent Foramen Ovale Closure System compared to anticoagulation therapy at 12 months

### TECHNICAL APPROACH

The experimental part of the procedure in the investigational group will be the use of the CARDIA STAR™ System closure procedure and all the medications given are part of the standard clinical procedure.

These subjects will be broken into two groups: (1) the Roll-In group (200 patients) and (2) the study group (300 patients). Roll-In subjects are done as training cases for physicians. These subjects are not randomized, but must meet all of the inclusion/exclusion criteria of the study. Informed consent is also required for all Roll-In patients. The follow-up for these patients will be identical to that of the device group patients in the study group. Study subjects will be randomized 1:1 to one of two treatment groups: (1) those who receive a CARDIA STAR™ device and (2) those who receive anticoagulation therapy for 12 months. The second group will serve as the control group since anticoagulation therapy is standard for this patient population. All subjects will be followed for one year.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Warfarin Versus Aspirin In Reduced Cardiac Ejection Fraction (WARCEF)

KEYWORDS:

PRINCIPAL INVESTIGATOR: Welka, Stephen, MAJ MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: N

SERVICE: Cardiology

INITIAL APPROVAL DATE: 8 April 2003

### STUDY OBJECTIVE

The primary objective of the study is to determine whether warfarin (International Normalized Ratio [INR] 2.5-3.0, target INR 2.75) or aspirin (325 mg per day) is superior for preventing all-cause mortality and stroke combined in patients with ejection fraction (EF) < 30%, when balanced against any risk of intracerebral hemorrhage.

### TECHNICAL APPROACH

This is a multi-center, randomized, double blind study. Baseline testing will be done before randomization. Subjects will have a complete medical history taken, a physical examination, blood tests (approximately 4 teaspoons taken), and echocardiogram as part of standard of care. Women of childbearing potential will have a urine pregnancy test before beginning the study for research purposes. If the requirement criteria are met, the subject will be randomized to one of two groups. Each patient will receive two medications.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Protocol XRP4563B/4001 - A Prospective, Open-Label, Randomized, Parallel-Group Investigation to Evaluate the Efficacy and Safety to Enoxaparin Versus Unfractionated Heparin in Subjects Who Present to the Emergency Department with Acute Coronary Syndrome

KEYWORDS:

PRINCIPAL INVESTIGATOR: MAJ Daniel Simpson, MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Cardiology

STATUS: N  
INITIAL APPROVAL DATE: 15 July 2003

STUDY OBJECTIVE

See page 14, section 2, of the sponsor's protocol.

TECHNICAL APPROACH

This study will be conducted using the drug, enoxaparin (Lovenox®). Enoxaparin has been approved by the Food and Drug Administration (FDA) for the prevention of ischemic complications of unstable angina and non-Q wave myocardial infarction. The drug has not been approved for use for patients with acute coronary syndrome coming into the emergency department. Pursuant to AR 40-7, paragraph 4-12, "Use of an Approved Drug for an Unapproved Indication," this study does not require the acquisition of an IND number from the FDA. All conditions listed in this paragraph as "a-e" are met by this clinical investigation. Additionally, Department of Health and Human Services "Investigational Use of Marketed Products" guidelines, dated February 1989, indicates an IND number is not required in the conduct of this study.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Pulsus Paradoxus in Central Obesity

KEYWORDS:

PRINCIPAL INVESTIGATOR: Joseph C. Lee, CPT, MC

ASSOCIATES: John E. Atwood, COL, MC; Allen J. Taylor, LTC, MC

DEPARTMENT: Medicine

STATUS: N

SERVICE: Cardiology

INITIAL APPROVAL DATE: N/A

### STUDY OBJECTIVE

Determine whether abdominal obesity is associated with pulsus paradoxus.

Assess the accuracy of the measurement of pulsus paradoxus by sphygmomanometry.

Assess the accuracy of bedside measurement of neck veins as they may reflect right atrial pressures.

Investigate the mechanism for neck vein distention with abdominal compression.

### TECHNICAL APPROACH

Up to 170 military health care beneficiaries age 18 years and older presenting for elective outpatient cardiac catheterization will be studied for the presence of pulsus paradoxus in the setting of central obesity. This will be a prospective observational study to assess for the presence of pulsus paradoxus in study participants with central obesity. In selected patients also undergoing right heart catheterization, we will also assess the relationship between neck vein height and right atrial pressures. We will also observe the mechanism for jugular venous distention in the setting of abdominal compression. We will also be investigating for a relationship between central (or abdominal) obesity with pulsus paradoxus (abdominal or central obesity referring to patients with prominent adipose tissue collection around the abdomen). Hence we will be taking measurements of the abdomen at various locations. The level at which the circumference of the abdomen becomes significant enough to cause a pulsus paradoxus to develop has not been defined and would be investigated in this protocol.

Our primary endpoint is to document an exaggerated drop in systolic blood pressure with inspiration in patients with central obesity. Hence, our independent variable will be the transverse circumference of the patients' body. Our dependent (outcome) variable will be the degree of pulsus paradoxus present.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Quantitative Assessment of Cyclooxygenase-2 Gene/mRNA Expressions in Paraffin Embedded Benign and Cancerous Thyroid Tissues

KEYWORDS:

PRINCIPAL INVESTIGATOR: Vaishnav, Yashesh N., Ph.D. DAC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Endocrine

STATUS: N  
INITIAL APPROVAL DATE: 15 April 2003

### STUDY OBJECTIVE

To identify activation of the potential cancer gene cyclooxygenase-2 (COX-2) in paraffin embedded thyroid cancer tissues.

To explore if we can quantitatively amplify expression levels of COX-2 mRNA from benign and cancerous paraffin embedded thyroid tissues.

To determine whether the expression levels of COX-2 mRNA isolated from paraffin embedded thyroid cancer tissues can be used as a marker for diagnosis of different subclasses of thyroid cancer in patients.

### TECHNICAL APPROACH

This is a three-part study. Part 1 is a pilot study where we will be examining the feasibility of these studies to assess expression levels of COX-2 protein utilizing IHC staining procedure for the normal and cancerous tissue specimens. In Part 2, we will quantitatively assess COX-2 mRNA in paraffin embedded benign and cancerous tissues utilizing QT-RT-PCR technology. In Part 3, we will correlate expression levels of COX-2 mRNA in normal and cancerous thyroid tissue and will analyze and correlate the data statistically for the different subclasses of thyroid cancer.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

**TITLE:** A One-Year, Open, Randomized, Parallel, Three-Arm Study Comparing Exubera® (Insulin Dry Powder Pulmonary Inhaler) vs. Avandia® (Rosiglitazone Maleate) as Add-On Therapy vs. Exubera® Substitution of Sulfonylurea in Patients with Type 2 Diabetes, Poorly Controlled, On Combination Sulfonylurea and Metformin Treatment

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** Vigersky, Robert A., COL MC  
**ASSOCIATES:**

**DEPARTMENT:** Medicine  
**SERVICE:** Endocrine

**STATUS:** N  
**INITIAL APPROVAL DATE:** 10 June 2003

### STUDY OBJECTIVE

See attachments to original protocol submission, page 5.

### TECHNICAL APPROACH

The drug to be used in this study, Exubera® (insulin dry powder pulmonary inhaler), is investigational and will be used under IND number 43,313, which is held by Pfizer Pharmaceuticals, Inc. A copy of the Investigator's Brochure is on file in the Research Review Service, Department of Clinical Investigation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Evaluation of Somatostatin Receptor (SSTR) Response to rh TSH in Various Thyroid Cancer Cell Lines

KEYWORDS:

PRINCIPAL INVESTIGATOR: Robbins, Iris, Medical Technician  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Endocrine

STATUS: N  
INITIAL APPROVAL DATE: 5 August 2003

### STUDY OBJECTIVE

Assess change in expression of Somatostatin Receptor (SSTRs 2, 3, and 5) in human thyroid cell lines exposed to various concentrations of rh TSH.

### TECHNICAL APPROACH

Only well established human cell lines already generally available will be utilized for this project.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: The Effect of Bowel Preparation in Wireless Capsule Endoscopy (WCE)

KEYWORDS:

PRINCIPAL INVESTIGATOR: Napierkowski, John, MAJ MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: N

SERVICE: Gastroenterology

INITIAL APPROVAL DATE: 22 October 2002

### STUDY OBJECTIVE

To compare the quality of images obtained with wireless capsule endoscopy (WCE) following a standard bowel preparation versus a purgative bowel preparation. Our hypothesis is that the quality of image will be enhanced by a purgative bowel preparation enabling the gastroenterologists to detect lesions that might otherwise be obscured by retained bubbles, liquid, or solid stool. This is a two-part study.

### TECHNICAL APPROACH

Ten normal male and female volunteers and ten male and female patients with obscure gastrointestinal bleeding and normal upper and lower endoscopies will be recruited to participate. Participants will be recruited from within the National Capital Health Care system. The first part of the study will involve control subjects who do not have suspected intestinal blood loss. The second part of the study will involve patients referred for the WCE exam for the evaluation of gastrointestinal blood loss of obscure origin. WCE is an approved clinical tool for the evaluation of obscure GI bleeding and is currently being used in the GI clinic. The volunteers will be informed of the purpose of the study. They will be informed that study participation involves three visits. They will be given a form labeled "Wireless Capsule Endoscopy Timeline". At first visit, a history and physical exam will be performed. The second visit will involve the first of two WCE exams. The individual will be asked to return after eight hours or upon passage of the Capsule, malfunction of the equipment, or the development of symptoms such as nausea or abdominal pain. When the volunteers return, the equipment will be removed and they will fill out a questionnaire. The third visit will occur about two weeks later, and will involve the same timeline as outlined for the WCE exam. The WCE exams will be reviewed and graded by endoscopists who are blinded to the type of preparation used. Two independent reviewers trained in reading WCE images will be blinded to the type of preparation and will evaluate the quality of the images. Images of each quartile of the small bowel will be graded on a scale of 1 to 10, with 1=<10% visibility and 10-100% visibility of the intestinal mucosa. The reviewers will also grade the overall quality of each WCE.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Prospective Comparison of a New Immunochemical Fecal Occult Blood Test, !nSURE™, With Standard Guaiac, Fecal Occult Blood Sampling, Hemocult

KEYWORDS:

PRINCIPAL INVESTIGATOR: Sachar, David CPT MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Gastroenterology

STATUS: N  
INITIAL APPROVAL DATE: 14 January 2003

### STUDY OBJECTIVE

To prospectively compare the sensitivity and specificity of a new immunochemical fecal occult blood assay, !nSure™ (Enterix, Falmouth, ME) with a standard guaiac fecal occult blood sampling assay, Hemocult®, (Beckman Coulter, Palo Alto, CA).

### TECHNICAL APPROACH

Up to 1500 military health care beneficiaries between the ages of 49 to 80 years presenting for routine screening colonoscopy will be studied. Patients will be recruited and enrolled at WRAMC. This is a prospective, paired direct comparative study of the two FOBTs in a screening population. Each subject who participates will take stool samples for each of the two FOBTs to be compared, from sequential bowel movements, and then undergo a routine screening colonoscopy two weeks later. Although colonoscopy is considered a routine clinical test, the information from the procedure will also be used for research purposes within the context of this study. The !nSure™ assay is the only test/procedure in this protocol that is not considered standard of care and is being performed for research purposes.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Antibiotic Therapy For The Treatment of Crohn's Disease – A Double Blind, Placebo Controlled Trial

KEYWORDS:

PRINCIPAL INVESTIGATOR: Sachar, David CPT MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Gastroenterology

STATUS: N  
INITIAL APPROVAL DATE: 11 March 2003

### STUDY OBJECTIVE

The purpose of this study is to test if antibiotic medications directed against the bacterium *M. paratuberculosis* will cure Crohn's disease.

### TECHNICAL APPROACH

This is a multi center study of 136 patients with active Crohn's disease, defined as a Crohn's Disease Activity Index (CDAI) of  $\geq 151$  points. The CDAI is paired with the endoscopic index of severity (colonoscopy). At baseline and study months 12 and 24, two short visits will be needed to facilitate and support the colonoscopy procedure and for the balance of study activities assigned to that time point. The CDAI diary will be given to subjects during this baseline visit and returned at the 12 and 24 month visits. The CDAI calculation will be completed at this point. Subjects will be part of the study for two years. Fourteen visits will be scheduled during this time. Multiple outcome variables will be monitored.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: The Use of Multichannel Intraluminal Impedance (MII) to Assess the Proximal Extent of Gastroesophageal Reflux In Patients With Severe Gastroesophageal Reflux

KEYWORDS:

PRINCIPAL INVESTIGATOR: Mulhall, Brian P., MAJ MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Gastroenterology

STATUS: N  
INITIAL APPROVAL DATE: 25 March 2003

### STUDY OBJECTIVE

To correlate the extent of proximal reflux flow by scintigraphy and MII.

To correlate the volume clearance time between scintigraphy, manometry pH, and MII. This will especially look at clearance time for episodes where pH<4.

To correlate the ability of these technologies to quantify volume of reflux during a reflux episode between scintigraphy and MII.

To assess the ability of MII to determine the direction of flow during an RE.

### TECHNICAL APPROACH

This is an observational pilot study to assess the performance parameters of a new FDA-approved technology. Up to ten patients with severe GERD will be enrolled in this study in two arms. The first arm is the scintigraphy arm and will include six people. The second arm is the fluoroscopy arm and will include up to four people. For either arm, once consented and enrolled, patients will present to the GI Clinic at WRAMC to undergo placement of a combined manometry, pH, and MII probe placed nasally into their proximal and distal esophagus.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Colon Cancer – Non-Invasive Isolation Technology

KEYWORDS:

PRINCIPAL INVESTIGATOR: Duncan, Marten, CPT MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: N

SERVICE: Gastroenterology

INITIAL APPROVAL DATE: 1 April 2003

### STUDY OBJECTIVE

To assess the sensitivity and specificity of specific biomarkers on isolated conolococytes in identifying colon cancer and polyps confirmed by colonoscopy and to develop a standardized kit for the detection of colon cancer, non-invasively, as a cost-effective screening tool.

### TECHNICAL APPROACH

This is an NIH Grant, cross-sectional observational study of patients undergoing routine colonoscopy at one of two medical centers: Sinai Hospital of Baltimore and the Walter Reed Army Medical Center in Washington DC. This study will be conducted over a period of two years. Tumor specific markers will be correlated with tumor grading and histological type using Spearman's correlation coefficient as well as calculation of sensitivity and specificity.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Exploring System- and Patient-Level Predictors of Adherence to Secondary Screening for Colorectal Carcinoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Mulhall, Brian P., MAJ MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Gastroenterology

STATUS: N  
INITIAL APPROVAL DATE: 8 April 2003

### STUDY OBJECTIVE

To establish the rate of adherence to defined surveillance regimens for individuals with known high-risk colorectal lesions (adenomas) at WRAMC and NNMC.

To compare the rates of adherence in these two different systems, WRAMC (a system without polyp registry) and NNMC (a system with a polyp registry).

To identify psychosocial factors that are associated with adherence to recommended screening strategies.

### TECHNICAL APPROACH

The initial phase is a cohort study assessing adherence in those individuals defined to have adenomas. These cases will be identified through a CHCS search that simply defines any cases found to have colorectal adenomas during this period, and we will only record the number of polyps, the histologic findings, the name and age of the patient, and the date of procedure. Once all records meeting these criteria have been identified, we will search the endoscopy records at either institution to assess which cases have had subsequent screening evaluations since that time.

The second phase includes questionnaire development. These individuals will be referred by their internist or gastroenterologist and will be informed of the purpose of the focus groups. During the meeting, these individuals will be asked to share their thoughts on various questions related to CRC and CRC screening.

The final phase (the mail-out questionnaire) is best defined as a cross-sectional survey of a cohort assessing for variables that may have impacted the eventual outcome of adherence to screening guidelines. Overall, this study is solely descriptive. Data input and analysis will be blinded to each individual's referent system or cohort group (adherent or non-adherent). We will then collect all questionnaires, tabulate the data, and complete analysis and manuscript preparation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: CALGB 500101/E4697 – A Randomized, Placebo-Controlled Phase III Trial of Yeast Derived GM-CSF Versus Peptide Vaccination Versus GM-CSF Plus Peptide Vaccination Versus Placebo In Patients With “No Evidence of Disease” After Complete Surgical Resection of “Locally Advanced” and/or Stage IV Melanoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 8 October 2002

### STUDY OBJECTIVE

Primary objective is to compare overall survival, two-year survival, and time to progression of patients with completely resected stage IV melanoma or stage III melanoma with gross extra nodal extension, satellites, and/or in transit lesions, treated with GM-CSF versus no GM-CS or other high risk patients. Secondary objective is to compare, using a 2x2 factorial design, overall survival, two-year survival, and time to progression of HLA-A2 positive patients treated with peptide vaccination versus no peptide vaccination.

### TECHNICAL APPROACH

HLA-A2 positive patients will be randomized to receive GM-CSF plus peptide vaccination, GM-CSF placebo plus peptide vaccination, GM-CSF plus peptide placebo, or GM-CSF placebo plus peptide placebo. HLA-A2 negative patients will be randomized to receive either GM-CSF or GM-CSF placebo.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: CALGB 49907/CTSU 49907 – A Randomized Trial of Adjuvant Chemotherapy With Standard Regimens, Cyclophosphamide, Methotrexate, and Fluorouracil 0 (CMF) or Doxorubicin and Cyclophosphamide – (AC) Versus Capecitabine in Women 65 Years and Older With Node Positive or High-Risk Node-Negative Breast

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: N

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 22 October 2002

### STUDY OBJECTIVE

Primary objective is to compare the effectiveness of standard chemotherapy regimens (CMF or AC) with single agent capecitabine with respect to disease free survival in women 65 years and older with local and regional breast cancer. Secondary objectives are:

- To compare effectiveness of standard chemotherapy regimens with capecitabine with respect to overall survival.
- To determine the effects of each treatment regimen on quality of life and physical function.
- To assess the toxicity of each treatment program.
- To study the adherence to an oral chemotherapy regimen in older patients.

### TECHNICAL APPROACH

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: CALGB 49909 – Phase III Trial of Doxorubicin and Cyclophosphamide (AC) Followed by Weekly Paclitaxel With or Without Trastuzumab as Adjuvant Treatment for Women With HER-2 Over expressing or Amplified Node Positive Breast Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 12 November 2002

### STUDY OBJECTIVE

The Phase III program is designed to establish the benefits and risks of Herceptin. The primary endpoint for the study is the duration of disease-free survival.

### TECHNICAL APPROACH

Herceptin is administered either as a single agent (H0649g) or in combination with chemotherapy (H0648g) to women with HER2-overexpressing metastatic breast cancer. This drug is experimental and investigational, and will be used under IND # 6667 which is held by Genentech Inc. Up to twenty female military health care beneficiaries age 18 years and older presenting with the diagnosis of HER-2 (a gene that has negative prognostic factors) positive breast cancer, with one or more positive lymph nodes, will be enrolled at WRAMC. A total of up to 3000 patients will be accrued study wide. Subjects will be recruited from the WRAMC Hematology-Oncology Clinic Breast Cancer Center and referred by their physicians. This study is a prospective, randomized, control Phase III trial and will use a dynamic allocation procedure to assign an equal number of subjects to one of the three treatment regimens. The stratification factors that will be used are the number of positive lymph nodes and receptor status.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: CALGB 89902 - Phase II Study Evaluating the Combination of 5-Fluorouracil, Leucovorin, Oxaliplatin (NSC #266046), and Herceptin (NSC #688097) in the Treatment of Patients with Metastatic Colorectal Cancer Who Have Progressed After 5-FU and/or Irinotecan-Containing Therapy

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: W  
INITIAL APPROVAL DATE: 12 November 2002

### STUDY OBJECTIVE

Study withdrawn.

### TECHNICAL APPROACH

Study withdrawn.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn.

### CONCLUSIONS

Study withdrawn.

## DETAIL SUMMARY SHEET

TITLE: CALGB 80003 – A Phase II Study of Gemcitabine, 5-Fluorouracil, and Radiation Therapy in Locally Advanced Non-Metastatic Pancreatic Adenocarcinoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 12 November 2002

### STUDY OBJECTIVE

Primary objective is to assess overall survival of patients with locally advanced pancreatic cancer who are treated with concurrent gemcitabine, 5-FU, and external beam radiation therapy. Secondary objectives are:

- Estimate time to progression in this patient population.
- Estimate overall clinical response to chemoradiation therapy in this patient population.
- Estimate the biomarker response to chemoradiation through evaluation of circulating CA 19-9 levels.
- Assess the toxicity associated with this regimen.

### TECHNICAL APPROACH

Open label, non-randomized, combination study of gemcitabine, 5-FU, and external beam radiotherapy in patients with locally advanced non-metastatic pancreatic cancer. All patients will be assessed by history and physical exam including weight, vital signs, and performance status within 14 days of initiation of therapy. Baseline hematologic, and biochemical profiles, including CBC with differential, alkaline phosphatase, bilirubin, SGOT (AST), BUN, creatinine, and CA 19-9 will be completed within 14 days of initial of therapy. During cycle 1 (chemoradiation), gemcitabine will be given weekly with continuous infusion of 5-FU delivered five of every seven days and concurrent external beam radiotherapy. Both gemcitabine and 5-FU will continue throughout the course of external beam radiation therapy and will be discontinued following the conclusion of external beam radiation therapy. All patients will have a central venous access device placed to facilitate chemotherapy administration. During cycles 2-5, gemcitabine will be administered at dose of 1000mg/m<sup>2</sup> over thirty minutes weekly for three weeks followed by one-week rest for four cycles.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: CALGB 90102 – A Phase II Study of Cisplatin, Gemcitabine, and ZD1839 (IRESSA) (IND # 61187, NSC 715055) For the Treatment of Advanced Urothelial Tract Carcinoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 12 November 2002

### STUDY OBJECTIVE

Primary objective is to describe overall response proportion in patients with advanced carcinoma of the urothelial tract treated with cisplatin, gemcitabine, and ZD1839, given on a 21 day schedule with a prolonged gemcitabine infusion, followed by maintenance ZD1839. Secondary objectives are:

- Describe time to progression, progression-free survival, and overall survival in patients.
- Evaluate effect of Epidermal Growth Factor Receptor (EGFR) expression level on overall response rate and progression-free survival.
- Assess the toxicity of the combination given on a 21-day schedule with a prolonged gemcitabine infusion, followed by maintenance ZD1839.

### TECHNICAL APPROACH

Chemotherapy (gemcitabine/cisplatin) plus ZD1839 (Combination Phase) will be followed by the ZD1839 only (Maintenance Phase). The Maintenance Phase will be initiated only if the disease stabilizes and there is partial or complete response. If the disease progresses, then the subject will be removed from the study. Tissue samples previously obtained from a biopsy of the tumor or surgery will be used for research testing of epidermal growth factor receptor (EGFR). If samples are not available, a biopsy will be done to obtain the sample.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: CALGB 79807-00 – Smoking Cessation Intervention [Including Bupropion (Zyban®) Versus Placebo] For Completely Resected Stage I and Stage II Non-Small Cell Lung Cancer Survivors Who Are Currently Smoker, Phase III

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 28 January 2003

### STUDY OBJECTIVE

To compare, separately in men and women, the effect on twelve-month quit rates of adding an anti-depressant called Bupropion (Zyban®) versus placebo in a double-blind fashion to a behavioral intervention and nicotine replacement in completely resected Stage I and II non-small cell lung cancer patients who are current smokers.

### TECHNICAL APPROACH

This is a randomized, multi-institution, double blind, placebo-controlled phase III study. Patients will be randomized to receive the stop-smoking program, the Nicotine Patch and placebo, or the stop-smoking program, Nicotine Patch, and Bupropion.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: CALGB 90008 – A Phase II Study of Capecitabine (IND # 62761) Plus Gemcitabine for Metastatic Renal Cell Carcinoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 28 January 2003

### STUDY OBJECTIVE

The main endpoint of this study is objective response rate (good and bad) for the combination of gemcitabine and capecitabine on patient and patient's kidney cancer. Secondary endpoints are toxicity, progression-free survival, and overall survival.

### TECHNICAL APPROACH

Subjects will be asked to give information regarding their medical history and undergo routine exams like physical exam, blood tests, CT scan, or MRI. Subjects will have an exam every four weeks to assess any symptoms from the cancer and any side effects from the treatment. Blood tests will be performed every week as standard of care.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: CALGB 79809 – Phase III Trial of Intravenous Zoledronic Acid (Zometa®) (IND #62751) in the Prevention of Bone Loss in Localized Breast Cancer Patients with Chemotherapy-Induced Ovarian Failure

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 27 May 2003

STUDY OBJECTIVE

This study will be conducted using the drug Zoledronic acid (Zometa®). Zometa® has been approved by the FDA for use in treating patients with multiple myeloma and patients with documented bone metastases from solid tumors in conjunction with standard cancer therapy. The drug has not been approved for use in reducing bone loss in the lumbar spine in premenopausal breast cancer patients.

TECHNICAL APPROACH

This is a randomized phase III trial to determine if intravenous Zoledronic acid administered every three months will reduce bone loss in the lumbar spine in premenopausal breast cancer patients age 40 years and older who are receiving adjuvant chemotherapy.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: NSABP Protocol B-33 - A Randomized, Placebo-Controlled, Double-Blind Trial Evaluating the Effects of Exemestane in Clinical Stage T<sub>1-3</sub> N<sub>0-1</sub> M<sub>0</sub> Postmenopausal Breast Cancer Patients Completing at Least Five Years of Tamoxifen Therapy

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 10 June 2003

### STUDY OBJECTIVE

Please see sponsor's protocol, page 26, section 3.0 for more detailed information.

### TECHNICAL APPROACH

This study will be conducted using the drug, exemestane (Aromasin®). Aromasin® has been approved by the FDA for use in the treatment of advanced stage breast cancer in postmenopausal patients. The drug has not been approved for use in treatment of estrogen-receptor-positive (ER+) and/or progesterone-receptor-positive (PgR+) breast cancer (T1-3 N0-1 M0) in postmenopausal patients.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: NSABP Protocol B-35 - A Clinical Trial Comparing Anastrozole with Tamoxifen in Postmenopausal Patients with Ductal Carcinoma in Situ (DCIS) Undergoing Lumpectomy with Radiation Therapy

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 10 June 2003

### STUDY OBJECTIVE

Please see sponsor's protocol, page 10, and section 3.0 for more detailed information.

### TECHNICAL APPROACH

This is a Phase III randomized, double-blind study to evaluate the effectiveness of Anastrozole compared to tamoxifen in preventing the subsequent occurrence of breast cancer (local, regional and distant recurrences, and contralateral breast cancer) in postmenopausal women with primary ductal carcinoma in situ (DCIS) treated with lumpectomy and breast radiation. Radiation therapy is standard of care for this patient population.

Subjects will be asked to give information regarding their medical history and undergo routine exams like a physical exam, blood tests, and mammogram and pelvic exam, if applicable, prior to study entry. These exams and test are routine and not experimental. Women of childbearing potential will have a urine pregnancy test for research purposes. Subjects will receive treatment in this study as outpatients. Subjects will be randomized to one of two treatment groups.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: CALGB 119901 - Quality of Life of African American Cancer Survivors

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: N

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 29 July 2003

### STUDY OBJECTIVE

To compare the quality of life between African American cancer survivors and African Americans who have not had cancer, who are similar in terms of age, gender, and socioeconomic status, and to determine the prevalence of cancer-related problems and their effects on quality of life and cancer screening behaviors.

### TECHNICAL APPROACH

This descriptive study utilizes a case-control design in which African American cancer survivors will be compared with a sample of African American controls who have not had cancer. The survivor sample will be composed of survivors of five types of cancers so that comparisons can be made across cancer types.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: SWOG S0023 – A Phase III Trial of Cisplatin/Etoposide/Radiotherapy with Consolidation Docetaxel Followed by Maintenance Therapy with ZD1839 (NSC 715055) or Placebo in Patients with Inoperable Locally Advanced Stage III Non-Small Cell Lung Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 29 July 2003

### STUDY OBJECTIVE

To compare the effects (both good and bad) of the combination of cisplatin, etoposide, and radiation followed by Docetaxel plus ZD1839 or placebo on non-small cell lung cancer.

### TECHNICAL APPROACH

Multicenter, prospective, double blind, randomized trial.

Methodology: This trial will employ three phases of treatment: 1) Induction, 2) Consolidation and 3) Maintenance. Each phase will be administered sequentially and will be dependent upon the patient's completion of the previous component and evaluation of the status of the disease. The agents involved with each of the treatment phases are as follows:

1. Induction - All subjects will receive Cisplatin and Etoposide.
2. Consolidation - Subjects with stable or better disease after completion of induction therapy will receive Docetaxel.
3. Maintenance - Subjects with stable or better disease after completion of consolidation therapy will be randomly assigned on a 1:1 ratio to ZD1839 or matching placebo capsule.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: SWOG S9925 – Lung Cancer Specimen Repository Protocol/Ancillary

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: N

SERVICE: Hematology-Oncology

INITIAL APPROVAL DATE: 29 July 2003

### STUDY OBJECTIVE

To establish a central lung center specimen repository to serve as a resource for current and future scientific studies.

### TECHNICAL APPROACH

Research design: Laboratory companion for SWOG S9900, S0003, and S0023 studies.

Methodology: Subjects will donate both tissue and blood samples obtained during the treatment portion of the study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: CALGB 80101 – Phase III Intergroup Trial of Adjuvant Chemoradiation After Resection of Gastric or Gastroesophageal Adenocarcinoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 29 July 2003

STUDY OBJECTIVE

See page 10, section 2.0 of the sponsor protocol.

TECHNICAL APPROACH

This is a prospective randomized treatment study. There will be blood tests every week during chemotherapy and chemoradiation therapy. The amount of blood taken for this study will vary from a finger stick to approximately three teaspoons. Women of childbearing potential must not be pregnant or breast-feeding due to the risk of toxicity in nursing infants. Women of childbearing potential will have a blood pregnancy test before the start of the study. Women of childbearing potential and sexually active males must use adequate contraception (hormonal or barrier method of birth control) prior to study entry and for the duration of study participation (including abstinence). These procedures are part of regular cancer care and may be done even if you do not join the study. If the patient agrees to participate in the laboratory studies associated with this study, a sample of blood that was taken at the time they were enrolled in the trial, and tissue that was taken at the time of surgery will be sent to a CALGB research laboratory. There will be some genetic testing done in the optional laboratory portion of this study for the patient who agrees to the use of their tissue and blood samples. The patient will be randomized to one of two treatment arms:

Arm A consists of 1 cycle of 5-FU and Leucovorin, followed by infusional 5-FU with concurrent radiotherapy, followed by 2 additional cycles of 5-FU and Leucovorin.

Arm B consists of 1 cycle of epirubicin, cisplatin, and infusional 5-FU (ECF), followed by infusional 5-FU with concurrent radiotherapy, followed by 2 additional cycles of ECF.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: CALGB 40105 – Evaluation of Novel Therapeutic Agents (Celecoxib: NSC #719627) Against Breast Cancer – An Innovative Randomized Phase II Trial Design

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 16 September 2003

### STUDY OBJECTIVE

To develop a novel phase II clinical trial design to test new agents in breast cancer that might not have detectable activity using the classic two-step phase II trial design.

### TECHNICAL APPROACH

Research design: Multicenter, prospective, double blind, randomized trial.

Methodology: Subjects will be randomized in a 2:1 ratio to receive either high dose (400 mg) or low dose (100 mg) celecoxib twice a day by mouth.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

**TITLE:** ECOG E1899 - A Phase III Randomized Trial for Evaluating Second Line Hormonal Therapy (Ketoconazole/Hydrocortisone) vs. Docetaxel/Estramustine Combination Chemotherapy on Progression Free Survival in Asymptomatic Patients with a Rising PSA after Hormonal Therapy for Prostate Cancer

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** Drabick, Joseph J., COL MC

**ASSOCIATES:** COL David G. McLeod, MC

**DEPARTMENT:** Medicine

**SERVICE:** Hematology-Oncology

**STATUS:** N

**INITIAL APPROVAL DATE:** 16 September 2003

**STUDY OBJECTIVE**

To evaluate the effectiveness of second line hormonal therapy (ketoconazole/hydrocortisone) vs. chemotherapy (Docetaxel, Estramustine) in asymptomatic patients with a rising PSA after hormonal therapy for prostate cancer.

**TECHNICAL APPROACH**

Research design: Multicenter, double blind, randomized trial.

Methodology: Subjects will be randomized to one of two treatment groups:

**Group A (Test Treatment)**

Participants will receive ketoconazole and hydrocortisone. Ketoconazole and hydrocortisone are the hormonal therapy arm of this study. Ketoconazole will be taken three times daily and the hydrocortisone twice daily.

**Group B (Test Treatment)**

Participants will receive Docetaxel and Estramustine phosphate (EMP). Docetaxel and Estramustine are the chemotherapy arm of this study. Estramustine phosphate (EMP) will be taken orally three times daily for five days every treatment cycle (each treatment cycle lasts three weeks). The Docetaxel will be administered by vein over one hour on Day 2 of each treatment cycle. On the days that Docetaxel is administered a steroid will also be administered to reduce possible side effects from occurring.

**PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE**

New Protocol for FY03.

**CONCLUSIONS**

## DETAIL SUMMARY SHEET

TITLE: Analysis of Banked Sera for Molecular and Biochemical Changes Associated With Development of Breast Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Flynn, Joseph M., CPT MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 22 October 2002

### STUDY OBJECTIVE

To identify and characterize proteins differentially expressed in serum of patients with breast cancer.

To identify and characterize any single nucleotide polymorphism, DNA amplification, and/or deletion in serum of patients with breast cancer.

To identify factors within patient serum-derived cellular components that correlate with patient risk factors or clinical status as defined in the corresponding clinical patient database.

### TECHNICAL APPROACH

We propose utilizing a novel approach to the study of breast tumor proteomics. Retrospective clinical data identified through the DMSS database will be identified on the basis of whether they have an associated breast cancer diagnosis. Each serum source evaluated in this protocol will also serve as an internal control since the design allows for serial evaluation of sera and thus changes over time will offer important internal comparisons. Specific numbers to be studied will be further established after a review of availability of serum by the AMSA staff.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: A Randomized Phase II Study of Thalidomide 200mg + Dexamethasone Versus Alone as Maintenance Therapy for Multiple Myeloma Following Autologous Bone Marrow Transplantation

KEYWORDS:

PRINCIPAL INVESTIGATOR: Waselenko, Jamie K., MAJ MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 12 November 2002

### STUDY OBJECTIVE

To investigate the feasibility, toxicity, and estimate the efficacy of maintenance therapy with dexamethasone with thalidomide 200mg in patients with multiple myeloma undergoing autologous transplants when compared to dexamethasone alone. To investigate the correlation of biologic markers of angiogenesis and apoptosis to response to therapy and relapse.

### TECHNICAL APPROACH

Patients will be evaluated six to nine months after their transplant procedure for their disease status. International Bone Marrow Registry criteria for assessment of response to autologous transplant in patients with multiple myeloma will be used to assess response. Medications will be withheld for any NCI grade 3 toxicity or higher attributable to them and not reversible or easily managed for standard supportive care such as antiemetics, antipyretics, and intravenous fluids or any medical complication of the transplant to which thalidomide is judged to be contributing.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Genomic and Proteomic Investigation for Pattern Differences in Gene and Protein Expression Between Diverse Primary Solid Tumors and Their Metastases from Paraffin-Embedded Pathologic Specimens

KEYWORDS:

PRINCIPAL INVESTIGATOR: Drabick, Joseph J., COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 1 April 2003

### STUDY OBJECTIVE

Using high throughput genomics and proteomics on archived paraffin-embedded tissue blocks to:  
Compare and contrast DNA aberrations and protein expression profile in primary tumors vs. their various metastases looking for common or distinguishing expression patterns.  
Determine if there are any expression features within a primary tumor that are suggestive of the development of metastasis to a particular site or not.  
Compare and contrast expression profiles for a given metastatic site between patients with the same cancer type and those with different cancers, looking for common patterns.

### TECHNICAL APPROACH

This is a correlative science study to be performed on archived tumor specimens from indirectly identified patients.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: An Open-Label, Multicenter, Randomized, Phase III Study Comparing Combination IV Topotecan/Docetaxel to Docetaxel Aline in Second-Line Advanced (IIIB/IV) Non-Small-Cell Lung Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Waselenko, Jamie K., MAJ MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Hematology-Oncology

STATUS: N  
INITIAL APPROVAL DATE: 30 September 2003

STUDY OBJECTIVE

To compare how patients who have previously received chemotherapy for their non-small cell lung cancer (NSCLC) respond to the combination of Hycamtin and Taxotere compared to Taxotere alone.

TECHNICAL APPROACH

Open-label, parallel, multicenter, randomized, active comparator phase III study.

Methodology: Subjects will be randomized to receive either:

- Hycamtin (IV) 3.5 mg/m<sup>2</sup>/day on days 1, 8 and 15 and Taxotere (IV) 30 mg/m<sup>2</sup>/day on days 1, 8 and 15, every 28 days, or
- Investigator choice of single-agent Taxotere (IV) administered either 75 mg/m<sup>2</sup>/day on day 1 every 21 days OR 35 mg/m<sup>2</sup>/day on days 1, 8 and 15 every 28 days.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03. This research has not received a DCI letter to begin the study.

CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Tc-99m Depreotide Scanning In Idiopathic Pulmonary Fibrosis

KEYWORDS:

PRINCIPAL INVESTIGATOR: Lettieri, Christopher CPT MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: N

SERVICE: Pulmonary & Critical Care Medicine

INITIAL APPROVAL DATE: 11 March 2003

### STUDY OBJECTIVE

To evaluate the frequency with which Tc-99m depreotide scanning is positive in patients with idiopathic pulmonary fibrosis. Specific objectives focus on exploring the significance of positive findings using Tc-99m depreotide scanning and include:

- Compare the imaging findings with the results of chest radiographs (CXRs) and other imaging modalities.
- Compare findings on Tc-99m depreotide with the presence of alveolitis.
- Compare the results of Tc-99 depreotide in patients with a clinical diagnosis of idiopathic pulmonary fibrosis to those who have a surgical lung biopsy showing usual interstitial pneumonia.
- Determine the interobserver variability of Tc-99m depreotide scanning in patients with idiopathic pulmonary fibrosis.

### TECHNICAL APPROACH

Clinical evaluation: Patients will undergo a history and physical by their pulmonary physician. Data routinely obtained in the evaluation of patients with IPF will be recorded. Outside of diagnostic tools previously established to evaluate patients with IPF, no additional testing other than the nuclear imaging will be required. No blood work will be done as part of this study. Patients will be clinically screened for acute pneumonia, which can create false positive results with depreotide scans. These patients will be excluded. Other pulmonic disease processes can result in positive results. However, these individuals would not carry the diagnosis of Idiopathic Pulmonary Fibrosis as a result of the other disease and would not be included in this study. The depreotide scan will be the only aspect of this trial that would not be routinely performed as part of clinical practice.

Specifically, we will record the presence or absence of activity in the parenchyma and activity in the hila. The physicians will be blinded to the clinical examination and clinical stage of the patient. The injection and imaging sequence are currently standard of care for patients with solitary pulmonary nodules.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Palatability Comparison of Children's Corticosteroid Suspensions – A Randomized Double-Blind Trial

KEYWORDS:

PRINCIPAL INVESTIGATOR: Norton, Scott A., LTC MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Dermatology

STATUS: N  
INITIAL APPROVAL DATE: 8 October 2002

### STUDY OBJECTIVE

To determine the palatability of eight different oral corticosteroid suspensions by having volunteers rate the palatability of each suspension on a Likert scale.

### TECHNICAL APPROACH

Oral corticosteroids are used to treat a variety of childhood conditions including nephritic syndrome, asthma, severe allergies, and skin diseases such as atopic and contact dermatitis. The formulation administered in young children is usually a liquid, and to ensure compliance special consideration should be given to taste. Often, parents observing their children provide the only available information on a medication's palatability. Oral suspensions of corticosteroids have a reputation for having a bitter unpleasant taste. Although several taste comparisons of different antimicrobial suspensions have been published, we are unaware of any study (randomized and blinded or otherwise) that compares the palatability of oral corticosteroid suspensions. Our study will attempt to assess the relative palatability of oral corticosteroid suspensions that in turn may help guide physician prescribing practices. The study may also influence pharmacy formularies including military hospitals.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Incidence of Bacteremia After Routine Teeth Brushing

KEYWORDS:

PRINCIPAL INVESTIGATOR: Wortmann, Glenn W., LTC MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Infectious Disease

STATUS: N  
INITIAL APPROVAL DATE: 26 November 2002

### STUDY OBJECTIVE

To determine the rate of bacteremia after tooth brushing.

To determine the temporal relationships of the bacteremia to the process of teeth brushing including the duration of the bacteremia.

To establish the incidence of bacteremia, the time at which it develops, and the duration of the bacteremia.

### TECHNICAL APPROACH

Participants will have a heparin lock inserted into a vein in the standard manner and an initial blood culture drawn. Participants will then be asked to brush their teeth for one minute. Repeat sets of blood cultures will be drawn through the heparin lock at 30 seconds and 20 minutes after completion of teeth brushing. After the final blood culture, patients will be referred to the Dental Clinic for an abbreviated dental exam and assign each participant a Gingival Index Score. During the course of the study, the investigators will check the results of the blood cultures every morning.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Isolation of Vaccinia From The Blood and Skin After Smallpox Vaccination

KEYWORDS:

PRINCIPAL INVESTIGATOR: Cummings, James F., MAJ MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: N

SERVICE: Infectious Disease

INITIAL APPROVAL DATE: 7 January 2003

### STUDY OBJECTIVE

Determine the rate and duration of vaccinia viremia after vaccination with smallpox vaccine. Determine if there is a difference in the rate and duration of vaccinia viremia between new vaccines and those who have been vaccinated previously. If virus is present, to determine if there is a correlation between clinical signs and symptoms and virus recovery. To determine the length of time it is possible to recover vaccinia from the smallpox injection site.

### TECHNICAL APPROACH

Fifteen patients will be randomly assigned to study group A and fifteen patients to study group B. Study group A will have blood drawn before vaccination and on days 1, 3, 5, 7, 9, 14, and 21 after vaccination. Study group B will have blood drawn before vaccination and on days 2, 4, 6, 8, 10, 14, and 21 after vaccination. If participants are systemically ill from the vaccination at day 21, we will continue to perform phlebotomy once a week until they are well, and then one additional time one week later. All blood draws will be performed plus/minus one day from the assigned day in order to allow for unexpected work absences.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Phase I/II Randomized Comparison of Localized Heat Therapy vs. Sodium Stibogluconate for the Treatment of Old World Cutaneous Leishmaniasis

KEYWORDS:

PRINCIPAL INVESTIGATOR: Aronson, Naomi E., COL MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Infectious Disease

STATUS: N  
INITIAL APPROVAL DATE: 24 June 2003

### STUDY OBJECTIVE

Primary Objective:

Assess safety, feasibility, and compare healing of local heat using Thermosurgery Technologies, Inc. (TTI) Thermo Med™ device versus sodium stibogluconate (SSG) IV 20mg/kg/d for 10 days, for treatment of cutaneous L. major infection (cure at two months after treatment started).

Secondary Objectives:

Compare healing of heat versus SSG in clinical response of all Leishmaniasis major skin lesions at 12 months after treatment initiated.

Compare toxicity profile of heat versus SSG treatment.

Determine feasibility of L. major species-specific polymerase chain reaction as a rapid diagnostic device in the context of a treatment trial.

Determine the immune response to Leishmania in both treatment arms:

- Flow cytometry
- Lymphocyte proliferation
- Cytokine profiles

### TECHNICAL APPROACH

A 2 arm, randomized trial of local heat therapy using ThermoMed™ device versus 10 days of systemic 20mg/kg/d sodium stibogluconate in the treatment of cutaneous old world Leishmaniasis. 27 patients per treatment arm, study duration 12 months.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: Prospective, Randomized Trial Comparing Continuous Lumbar Plexus Block and Sciatic Nerve Block Versus General Anesthesia for Total Hip Arthroplasty

KEYWORDS:

PRINCIPAL INVESTIGATOR: Buckenmaier, Chester C., LTC MC

ASSOCIATES: LTC John S. Xenos, MD, CPT Benjamin K. Potter, MD, MAJ Richard B. Islinger, MD

DEPARTMENT: Surgery

STATUS: N

SERVICE: Anesthesia-Operative

INITIAL APPROVAL DATE: 27 May 2003

### STUDY OBJECTIVE

To determine whether anesthetic technique affects clinical outcomes for total hip arthroplasty. (To compare outcomes and complications of the operative procedure and anesthetic technique for continuous peripheral nerve blockade versus general anesthesia for total hip arthroplasty.) The primary null hypothesis is that there is no significant difference between continuous peripheral nerve blockade and general anesthesia for total hip arthroplasty with regards to pain relief as measured by visual analog pain scores and questionnaires, intraoperative and postoperative blood loss as measured by operative record and drain output, and the incidence of early postoperative clinically significant deep vein thrombosis as assessed by Duplex ultrasound. Additionally, we will record and analyze secondary outcome measures such as postoperative nausea and vomiting, postoperative narcotic requirements, and perioperative complications of the procedure and the anesthetic techniques.

### TECHNICAL APPROACH

A prospective, randomized trial comparing continuous lumbar plexus block and sciatic nerve block versus general anesthesia for total hip arthroplasty.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: The Interaction Between Pyridostigmine Pretreatment and Neuromuscular Blocking Agents in *Rattus norvegicus*

KEYWORDS:

PRINCIPAL INVESTIGATOR: Mongan, Paul, LTC MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Anesthesia-Operative

STATUS: N  
INITIAL APPROVAL DATE: 27 June 2003

### STUDY OBJECTIVE

The null hypothesis: There is no change in duration of action of neuromuscular blockers in “patients” receiving pyridostigmine pretreatment.

### TECHNICAL APPROACH

The first experiment is to determine the best site for monitoring neuromuscular function in the rat. The second experiment will be a randomized controlled study using 80 rats to determine the effect of pyridostigmine pretreatment on the clinical effects of succinylcholine. The third experiment will follow number two with 1mg/kg of rocuronium IV substituted for succinylcholine, but otherwise it will be identical.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Ultrasound Assisted Lumbar Plexus Block

KEYWORDS:

PRINCIPAL INVESTIGATOR: Buckenmaier, Chester C., LTC MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Anesthesia-Operative

STATUS: N  
INITIAL APPROVAL DATE: 15 July 2003

### STUDY OBJECTIVE

Primary:

To compare and contrast LPB performed with prior ultrasound anatomy evaluation to LPB performed without ultrasound guidance.

To determine if prior ultrasound evaluation of lumbar anatomy can reduce the time required to complete a LPB and reduce the number of needle passes. Theoretically, a reduction in needle passes should correspond in reduced needle trauma and improved block safety.

Secondary:

To evaluate the utility of ultrasound in the performance of LPB.

### TECHNICAL APPROACH

The study population will consist of both male and female military health care beneficiaries 18 years and older presenting for a lower extremity orthopedic procedure requiring a lumbar plexus block who meet the inclusion criteria. Up to 48 patients will be asked to participate. The main endpoint of the study is to improve lumbar plexus block safety by reducing the number of needle passes necessary to place the block. The secondary endpoint is a reduction in time needed to place the block.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Prospective Randomized Study Comparing Sentinel Lymph Node (SLN) Evaluation With Standard Pathological Evaluation For The Staging of Colon Carcinoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Peoples, George E., LTC MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: General Surgery

STATUS: N  
INITIAL APPROVAL DATE: 22 October 2002

### STUDY OBJECTIVE

Define the rate of upstaging of colon carcinoma lymph node metastasis with SLN mapping. Null hypothesis: There is no difference in the rate of lymph node metastasis between conventional histopathological processing of lymph nodes and SLN mapping with detailed pathologic examination using immunohistochemistry (IHC) in patients undergoing resection of colon carcinoma.

### TECHNICAL APPROACH

Subjects will be randomly assigned in a 1:1 ratio to have either standard histopathological evaluation or SLN ultra staging (IHC) in conjunction with standard pathological evaluation utilizing a computerized built-in random assignment function. Only patients who wish to participate as subjects in this study, or the partner trial, Biological Relevance of Sentinel Lymph Node (SLN) Micrometastasis in Patients with Colon Carcinoma, will have the opportunity to have SLN mapping done on their specimens. The SLN pathology results will be made available to both the subject and the subject's physician. Subject participation will conclude with the surgical procedure. No follow-up is required for this clinical trial.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Molecular Phenotyping of Bone Marrow Aspirates and Peripheral Blood Collected As Part of The Walter Reed Army Medical Center Clinical Breast Care Project (CBCP)

KEYWORDS:

PRINCIPAL INVESTIGATOR: Stojadinovic, Alexander, MAJ MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: General Surgery

STATUS: N  
INITIAL APPROVAL DATE: 10 December 2002

### STUDY OBJECTIVE

The present study has two aims:

1. The acquisition and banking of peripheral venous blood and bone marrow aspiration specimens from informed and consenting donors to augment the existing tissue repository initiative. Blood and bone marrow specimens collected as part of this study will be added to the existing tissue repository established under WU 01-20006 and will be available for use for future unspecified research under 01-20006. The CBCP Tissue and Blood Library and the CBCP Director will be able to identify that these samples were collected as part of this separate molecular phenotyping protocol.
2. The application of modern functional genomic and proteomic technologies in order to discriminate normal from tumor cells in peripheral blood and bone marrow specimens on the basis of differential tumor-associated gene and protein expression alterations.

### TECHNICAL APPROACH

Collected specimens will be used for molecular, immunologic, biochemical, and histological investigations carried out at the CBCP labs. A credentialed provider will perform bone marrow aspiration. Bone marrow aspiration from both upper iliac crests will be performed using local anesthesia with monitored sedation, or if at the time of a scheduled surgical procedure, general anesthesia. Patients with and without breast cancer will participate in this study for the purposes of defining specificity of subsequent molecular profiling studies characterizing differential protein expression profiles between normal and malignant cells.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Phase 1b Trial of HER2/neu Peptide (E75) Vaccine in Node Negative Breast Cancer Patients

KEYWORDS:

PRINCIPAL INVESTIGATOR: Peoples, George E., LTC MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: General Surgery

STATUS: N  
INITIAL APPROVAL DATE: 10 December 2002

### STUDY OBJECTIVE

Assess safety and document local and systemic toxicity to the peptide vaccine (E75) in node negative breast cancer patients. Determine optimal doses of GM-CSF necessary to elicit an in vivo cellular immune response to peptide vaccine yet limit toxicity. Determine optimal inoculation schedule to elicit an in vivo cellular immune response to peptide vaccine. Correlate the efficiency of eliciting an in vivo cellular immune response to the peptide vaccine with the degree of HER2/neu expression in patient's tumor.

### TECHNICAL APPROACH

The goal is to vaccinate a total of sixty node negative breast cancer patients. These patients must be HLA-A2-positive. Although clinical recurrence is not a primary endpoint of this study since the expected incidence is low, we will follow the vaccinated patients and the HLA-A2- controls for clinical progression. Currently, all breast cancers have HER2/neu status determined during routine pathologic exams by FISH+/- immunohistochemistry. The patient's response to the vaccine will be correlated with the HER2/neu status of their tumor.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Clinical Use of Enterra™ Therapy System for Gastroparesis

KEYWORDS:

PRINCIPAL INVESTIGATOR: Brengman, Matthew, MAJ MC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: General Surgery

INITIAL APPROVAL DATE: 10 December 2002

### STUDY OBJECTIVE

The Gastric Electrical Stimulation (GES) System is indicated for the treatment of chronic, intractable (drug refractory) nausea and vomiting secondary to gastroparesis of diabetic or idiopathic etiology.

### TECHNICAL APPROACH

Only physicians who have completed the Medtronic sponsored courses will be allowed to refer for/implant/and follow the device. The procedure involves placement of electrical wires on to the stomach and a small generator device under the skin to provide electrical stimulation to the stomach. The leads will be placed on to the stomach with video assistance. The implantation of the neurostimulator will take place in an operating room and requires general anesthesia. The implant will take approximately one to three hours. Patient may remain hospitalized for 1-5 days following the procedure, depending on his or her medical condition. An endoscopy will be done during the implant of the device to help the surgeon locate the site where the leads should be implanted and to help decrease the risk of placing a hole in the stomach with the lead device. Follow up visits with the physician are important.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Biological Relevance of Sentinel Lymph Node (SLN) Micrometastasis in Patients With Colon Carcinoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Stojadinovic, Alexander, MAJ MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: General Surgery

STATUS: N  
INITIAL APPROVAL DATE: 28 January 2003

### STUDY OBJECTIVE

To determine the prognostic significance of molecular staging of colon carcinoma on the basis of sentinel lymph node mapping and analysis.

### TECHNICAL APPROACH

Primary colon cancer and regional nodal tissue from patients undergoing resection and SLN mapping using previously validated ex vivo blue dye techniques will be studied. Patients will undergo standard surgical resection of the colon cancer including the normal wedge of mesentery containing the draining lymphatics. The investigator will dissect all blue nodes from the mesentery. The primary tumor specimen with attached mesentery and the remaining half of the SLN(s) will be submitted to the Department of Pathology at WRAMC as separately labeled specimens. The unfrozen surgical specimen (colon and mesentery) will be sent to the WRAMC Department of Pathology for standard histopathological evaluation and staging of the cancer as per standard of care. DNA extraction and microsatellite instability will be conducted at CBCP Immunology and Research Laboratory at USUHS. RT-PCR for Cytokeratin-20 in SLN(s) will be conducted at the Memorial Sloan-Kettering Cancer Center. Cytokeratin immunohistochemistry testing results of the SLN will be reported as part of the WRAMC pathology report. All molecular data except the cytokeratin immunochemistry will be kept from the clinicians managing the patient as well as the research subject.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: A Prospective Functional Voice Assessment and Voice-Related Outcome Appraisal in Patients Undergoing Thyroid Surgery

KEYWORDS:

PRINCIPAL INVESTIGATOR: Stojadinovic, Alexander, MAJ MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: General Surgery

STATUS: N  
INITIAL APPROVAL DATE: 25 March 2003

### STUDY OBJECTIVE

The objectives of this study are:

To characterize the changes in voice following thyroid surgery using an objective functional voice instrument that relies on quantitative acoustic measures, the Dysphonia Severity Index (DSI).

To assess the level of functional impairment of voice following thyroid surgery using an outcome-base rating scale, the Voice Handicap Index (VHI).

To evaluate the natural history of acoustic voice changes (DSI) and voice-related quality of life (VHI) following thyroidectomy.

The analysis will be stratified according to nature of disease, extent of operation, laryngeal nerve identification, and use of intraoperative neuromonitoring.

### TECHNICAL APPROACH

This will be a prospective, non-randomized, single-arm study of patients with benign and malignant thyroid pathology who are candidates for primary thyroid surgery. The attending or resident physician will identify eligible patients and offer participation in the study. Patients will undergo rigid or flexible fiberoptic laryngoscopy pre-operatively to assess vocal cord function as part of standard of care assessment. Patients will undergo evaluation of the laryngeal structures and vocal function in the Army Audiology and Speech Center at Walter Reed Army Medical Center.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Is The Transforming Growth Factor-B Pathway Disrupted In Dermal Fibroblasts From Patients With CEAP 2-6 Chronic Venous Insufficiency?

KEYWORDS:

PRINCIPAL INVESTIGATOR: Gillespie, David L., LTC MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Peripheral Vascular Surgery

STATUS: N  
INITIAL APPROVAL DATE: 28 January 2003

### STUDY OBJECTIVE

Create a cell culture consisting of human dermal fibroblasts from normal thigh skin and diseased lower extremity skin in patients with chronic venous insufficiency.

Compare physical characteristics and expression of ligands and receptors using confocal microscopy in both cells and tissue samples.

Examine the expression of mRNA and protein of the mediators in diseased and normal human dermal fibroblasts.

Correlate experimental findings with clinical data to determine if there is an association between severity of disease and expression of ligands or receptors.

### TECHNICAL APPROACH

Subjects will serve as their own control to explore the expression of TGF- $\beta$  and its receptors, MMP 1 and 13, TIMP-1, Smad 3 and 4 in skin biopsies taken from normal skin of the thigh and diseased skin of the ankle in patients at WRAMC with venous insufficiency. In addition, these samples will be compared among the varying classifications of venous disease severity to determine if there are molecular differences along the spectrum of venous disease. Tissue samples will undergo processing to create a cell culture of human dermal fibroblasts.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: The Clinical Use of Neuroform™ Microdelivery Stent System – A Humanitarian Use Device  
Number H020002

KEYWORDS:

PRINCIPAL INVESTIGATOR: Armonda, Rocco MAJ MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Neurosurgery

STATUS: N  
INITIAL APPROVAL DATE: 25 February 2003

### STUDY OBJECTIVE

Safe obliteration of an intracranial aneurysm using minimally invasive neuroendovascular approach.

### TECHNICAL APPROACH

Full description of the surgical procedure is included in the Neuroform™ Stent documentation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Creation of an ICDB-Based Registry for Clinical Care on Military Patients with Spinal Cord and Spinal Column Injuries

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moquin, Ross, CDR MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Neurosurgery

STATUS: N  
INITIAL APPROVAL DATE: 28 January 2003

### STUDY OBJECTIVE

To create this database to be used as a clinic tool, enabling the physician and other patient care providers at the Walter Reed Army Medical Center (WRAMC) Neurosurgery Clinic to enter and extract patient medical information from a single source (to include radiology and laboratory results).

To assist the physician and staff in charting and completing letters to referring physicians in an efficient manner.  
To expedite the information gathering process by eventually allowing patients to input demographic and history type data into handheld devices.

To eventually utilize this database in retrospectively analyzing the diagnosis, treatments and treatment outcomes of patients at the Neurosurgery Clinic.

To determine the effectiveness and relative cost efficiency of treatment and rehabilitation strategies of spinal cord and column injuries (SCCI) now in use and to define optimal care of these patients.

### TECHNICAL APPROACH

The database will be a windows based relational database. The dual utilities of the database will be:

1. The database will serve as a central registry for patient care. Information which will be stored in the database will include patient demographic information as well as information about the patient's symptomology, diagnosis, treatment, and outcome. The information will be gathered from the patient and from the patient's medical records. It is anticipated that eventually the Neurosurgery Clinic will have the technology to allow patients to enter their own personal data into handheld devices linked to the database (similar to the already used point of service questionnaires used throughout many clinics at WRAMC).
2. The database will serve as an extremely effective research tool. It will provide the ability to retrospectively query specific patient data for the purpose of research.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Cage Instrumentation in Cervical Spine Surgeries: A Critical Review of Over 100 Cases

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moquin, Ross, CDR MC

ASSOCIATES: Rosner, Mike, MAJ MC

DEPARTMENT: Surgery

SERVICE: Neurosurgery

STATUS: N

INITIAL APPROVAL DATE: 23 September 2003

### STUDY OBJECTIVE

To evaluate the safety and efficacy of cervical spine reconstruction with anterior titanium mesh cages by reporting patient postoperative cervical fusion rates.

### TECHNICAL APPROACH

The purpose of this study is to evaluate the safety and efficacy of cervical spine reconstruction with anterior titanium mesh cages by reporting postoperative patient cervical fusion rates. This study will be conducted as a retrospective review of medical records and radiography of patients that have undergone this surgery six or more months prior to the study.

Over 100 charts will be reviewed for information regarding the patients' preoperative diagnoses, surgeries, and postoperative outcomes. Preoperative and postoperative radiography will be reviewed by a radiologist for evidence of cervical fusion.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Comparison of a Single Monocular Trial to Repeated Monocular Pressure Measurements in Determining The Effectiveness of a Topical Pressure-Lowering Medication

KEYWORDS:

PRINCIPAL INVESTIGATOR: Hammond, Matthew D., CPT MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Ophthalmology

STATUS: N  
INITIAL APPROVAL DATE: 26 November 2002

### STUDY OBJECTIVE

Is a monocular trial as useful as multiple monocular measurements in determining if a pressure-lowering drug is effective? Is there a difference between methods if a first, second, or third agent is being added? Is there a difference between methods if a certain type of medication is being added compared to other types of medications?

### TECHNICAL APPROACH

This study is a prospective data collection study. All patients will be in the same group. Each patient will have approximately 5-6 visits over the course of the study, with a total time frame of three to six months. The medication will be deemed effective based on the pre-medication target set by the treating physician. Also, at this point, if the medication is deemed ineffective based on the clinician's target, a second medication will be added, and these patients will have completed the current study outline. Those patients with bilateral glaucoma would also begin treatment of the second eye at this visit as well. The data from all the visits will then be divided into two groups - the "Monocular trial data group" and the "Multiple repeat measurement group".

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Accurate Diagnosis and Effective Management of Vitreoretinal Lesions Using Indirect Ophthalmoscopic Video Imaging

KEYWORDS:

PRINCIPAL INVESTIGATOR: Dick, John S., COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Ophthalmology

STATUS: N  
INITIAL APPROVAL DATE: 15 April 2003

### STUDY OBJECTIVE

The objective of this project is to demonstrate the useful application of a new technology. Validation of the indirect Ophthalmoscopic video imaging system will expand the scope and greatly enhance the role that tele-ophthalmology will play in the diagnosis and management of ocular disease and trauma.

### TECHNICAL APPROACH

The new technology that will be used is a newly available modification of the head-mounted binocular viewing system (indirect ophthalmoscope) that is already familiar to all ophthalmologists. The indirect ophthalmoscope used as part of this project is fitted with a small coaxial digital video camera that captures the entire examination on a digital camcorder. This equipment is portable and imaging can be obtained on a cooperative patient and on a prone patient under anesthesia. The digital video record of the examination can be viewed, edited, and transferred (tele-ophthalmology) to a remote location for expert interpretation by a consulting retina specialist.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Effect of Brimonidine Tartrate Ophthalmic Solution 0.15% on Pupil Diameter in Normal Eyes

KEYWORDS:

PRINCIPAL INVESTIGATOR: CPT John E. Thordsen, MC

ASSOCIATES:

DEPARTMENT: Surgery

SERVICE: Ophthalmology

STATUS: N

INITIAL APPROVAL DATE: 24 June 2003

### STUDY OBJECTIVE

To evaluate the effect of brimonidine tartrate ophthalmic solution 0.15% (Alphagan P) on pupil diameter under different luminance conditions. We hypothesize that the 0.15% solution of brimonidine tartrate possesses similar miotic properties as has been previously published for the 0.2% solution of brimonidine tartrate.

### TECHNICAL APPROACH

Our study is a prospective observational trial to evaluate the miotic (pupil constricting) effects of brominidine tartrate 0.15% for research purposes. About one week prior to the study, the principal investigator will consent each patient, review their medical history, check their heart rate and blood pressure and perform a baseline (undilated) eye exam which will include visual acuity, intra ocular pressure check, pupil reaction test and anterior segment exam - all of which are standard of care. The day or time interval between the consent/screening process and the actual day of the study can not be specifically identified, but will be largely based on looking at our clinic work schedule and picking a day when all of the staff/residents will be at the clinic. The best estimation between the screening process and the actual day the study will be carried out is about a week. Once the day of the study is chosen, all the study participants will be notified of the date.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: In Vitro Susceptibility of Acanthamoeba Species to WR99210, WR096268 and Analogues

KEYWORDS:

PRINCIPAL INVESTIGATOR: CPT Matthew D. Hammond, MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Ophthalmology

STATUS: N  
INITIAL APPROVAL DATE: 22 July 2003

### STUDY OBJECTIVE

To determine susceptibility of Acanthamoeba isolates to WR99210, WR096268 and analogues.

### TECHNICAL APPROACH

Acanthamoeba isolates from the American Type Culture Collection (ATCC) will be cultured on non-nutrient agar plates prepared in Page saline, with surface of the plate seeded with heat-killed (65 degrees Celsius © for 30 minutes) ATCC strain of Escherichia coli 25922 (Nna-E.coli). The plates will be incubated in a moist chamber aerobically at 37 degrees C and will be examined daily under a 10x objective in a bright field binocular microscope. When the cysts are formed in large numbers from the multiplying trophozoites, they will be harvested in 1 mL of Page saline and stored at 4 degrees C until used for antiamoebic drug susceptibility tests. All isolates will be nonaxenic and in the cystic form and will be held over at 4 degrees C until tested.

The stock strains of Acanthamoeba isolates will be cultivated as described above. The mature cysts will be gently scraped off using sterile disposable plastic bacteriologic loops, suspended in 1 mL quarter-strength Ringer lactate solution, washed thrice, and the pellet will be resuspended in 1 mL of the same buffer solution. The number of cysts will be counted using a hemocytometer, and the cyst suspension will be adjusted using the buffer to a final concentration of  $10^4$  cysts/mL.

All Acanthamoeba isolates will be tested against the current standards, PHMB (Apotheek, Westblank, NY, U.S.A.), and Chlorhexidine (ICN, Costa Mesa, CA, U.S.A.) as well as WR99201, WR096268 and analogue compounds from the WRAMC repository. Any compounds deemed potent will then be tested amongst themselves to determine the most potent compound. The tests will be designed to determine the minimum cysticidal concentration (MCC) of the drug.

Dilutions of PHMB, Chlorhexidine, WR096268 and WR99210, and other analogues will be made. The MCC will be defined as the lowest concentration of drug test solution that resulted in no excystment and the growth of trophozoites from Acanthamoeba after seven days of incubation. The results will be compared with the positive control, which should show the appearance of trophozoites within 24-48 hours of incubation on the inoculated NNA-E. coli plates. The observers of the results will not be masked from the concentrations of the drugs used in the tests.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Anatomic Correlation of Two Trigger Digit Injection Techniques

KEYWORDS:

PRINCIPAL INVESTIGATOR: Lenhart, Martha, LTC MC

ASSOCIATES:

DEPARTMENT: Orthopaedics and Rehabilitation

STATUS: N

SERVICE: Orthopedics Surgery

INITIAL APPROVAL DATE: 1 October 2002

### STUDY OBJECTIVE

We propose to examine and describe the hand anatomy as it relates to two injection techniques.

### TECHNICAL APPROACH

Twelve cadaver hands supplied by the anatomy section at USUHS will be used. The digits of cadaver hands will be injected using both the palmar and midlateral approaches. Both techniques will be used for each digit so that digits will be their own controls. Dissection around the needle will be performed with special attention to the anatomic relationship of neurovascular structures. Anatomic structures at risk will be detailed, photographed, and measured (mm between neurovascular structures and needle). The photographs will show the needles in place for visual demonstration of anatomic structures at risk.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Measurement of Distal Lower Extremity Tibiofibular Syndesmosis – Evaluation of Validity and Intraobserver and Interobserver Variability

KEYWORDS:

PRINCIPAL INVESTIGATOR: Pollock, Patrick J., CPT MC  
ASSOCIATES:

DEPARTMENT: Orthopaedics and Rehabilitation  
SERVICE: Orthopedics Surgery

STATUS: N  
INITIAL APPROVAL DATE: 1 October 2002

### STUDY OBJECTIVE

To evaluate the validity and inter/intra observer reliability of specific radiographic measures in humans with distal lower extremity (tibiofibular) syndesmosis (DLES) injuries.

### TECHNICAL APPROACH

The experimental design for this study will consist of a total of 32 individual, non-paired, fresh-frozen specimens. Three raters will evaluate six radiographic measurements at four conditions in each of the 32 specimens. Each of the three raters will view three different views (AP, M, L) with a total of six measurements between the three views. Total number of films to be printed for the study would be 32 (specimens) x 3 (views) x 4 (conditions) = 384 films. We will obtain 36 total specimens to account for error and practice.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Subaxial Cervical Spine – Biomechanical Analysis of Primary and Salvage Lateral Mass Screws Versus Pedicle Screws

KEYWORDS:

PRINCIPAL INVESTIGATOR: Potter, Benjamin, CPT MC  
ASSOCIATES:

DEPARTMENT: Orthopaedics and Rehabilitation  
SERVICE: Orthopedics Surgery

STATUS: N  
INITIAL APPROVAL DATE: 15 October 2002

### STUDY OBJECTIVE

To biomechanically test two commonly used means of hardware fixation to the subaxial cervical spine. It is our belief that pedicle screw fixation to the subaxial (C3-C7) cervical spine will prove to be biomechanically superior to lateral mass screw fixation in both primary and salvage applications. Subaxial cervical spinal fusions are indicated for a variety of cases, ranging from trauma to infection/tumor. It is our goal to measure the pull out strengths of two screw placement techniques to identify which insertion technique affords the strongest degree of fixation to the subaxial cervical spine.

### TECHNICAL APPROACH

This study is a two-stage study with the expectation that reportable data will be obtained at the conclusion of each mutually exclusive stage. Overall, the data will be reported to confirm or deny the null hypothesis that there is no difference in the mean pull strength, peak insertional torque, and safety for cervical pedicle screws versus lateral mass screws.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Request For the Clinical Use of The OP-1 Implant Humanitarian Use Device (HUD)

KEYWORDS:

PRINCIPAL INVESTIGATOR: Farber, Gerald, LTC MC

ASSOCIATES:

DEPARTMENT: Orthopaedics and Rehabilitation

STATUS: W

SERVICE: Orthopedics Surgery

INITIAL APPROVAL DATE: 22 October 2002

### STUDY OBJECTIVE

Study withdrawn.

### TECHNICAL APPROACH

Study withdrawn.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn.

### CONCLUSIONS

Study withdrawn.

## DETAIL SUMMARY SHEET

TITLE: Neurological and Sociodemographic Factors Affecting Gait, Function, and Quality of Life in Children and Adolescents With Myelomeningocele – A Comparison Between Multiple Centers

KEYWORDS:

PRINCIPAL INVESTIGATOR: McHale, Kathleen A., COL MC  
ASSOCIATES:

DEPARTMENT: Orthopaedics and Rehabilitation  
SERVICE: Orthopedics Surgery

STATUS: N  
INITIAL APPROVAL DATE: 28 January 2003

### STUDY OBJECTIVE

Determine role of motor paresis (according to motor level) and other possible causative factors. Establish whether the ambulatory function is correlated to health related quality of life in children with myelomeningocele.

### TECHNICAL APPROACH

This is a cross-sectional study that will be performed by two unbiased observers in collaboration with the treating physicians. The first part of the study will consist of the clinical exam. The second part of the study consists of gait analysis. Additional necessary basic data will be obtained for making decisions in choosing the type for treatment aimed at optimizing the ambulatory function of each subject.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Prospective Pediatric Scoliosis Study

KEYWORDS:

PRINCIPAL INVESTIGATOR: Kuklo, Timothy R., LTC MC  
ASSOCIATES:

DEPARTMENT: Orthopaedics and Rehabilitation  
SERVICE: Orthopedics Surgery

STATUS: N  
INITIAL APPROVAL DATE: 11 February 2003

### STUDY OBJECTIVE

The main objective of this study is to assess outcome measures in patients with pediatric idiopathic scoliosis (PIS) being treated with current surgical techniques. To reflect current operative techniques, consecutive patients with PIS treated surgically will be collected from spinal deformity centers with appropriate case volume, research capabilities, and study commitment. This prospective study will be able to: 1) Determine how accurately different spine surgeons classify Cobb curves, and 2) Develop a model to determine the most successful treatment for different classifications and patient characteristics.

A secondary objective of this study is to obtain data on currently available surgical approaches to treat PIS in the thoracic, thoracolumbar, and lumbar spine.

### TECHNICAL APPROACH

This is a prospective study that is an extension of the retrospective study entitled: Adolescent Idiopathic Scoliosis Single Overhang Curve (WU # 01-24006). Each participating surgeon will be asked to request participation of consecutive surgical patients with a diagnosis of pediatric idiopathic scoliosis in the thoracic, thoracolumbar, and/or lumbar spine.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Surgical Correction of the Distal Metatarsal Articulation Angle in Hallux Valgus – A Comparison of Common Metatarsal Osteotomies

KEYWORDS:

PRINCIPAL INVESTIGATOR: Pollock, Patrick J., CPT MC  
ASSOCIATES:

DEPARTMENT: Orthopaedics and Rehabilitation  
SERVICE: Orthopedics Surgery

STATUS: N  
INITIAL APPROVAL DATE: 18 March 2003

### STUDY OBJECTIVE

To compare the correction potential of four common hallux valgus osteotomies as measured by radiographic correction of the distal metatarsal articulating angle. To evaluate the inter/intra observer reliability of common radiographic measurements in hallux valgus.

### TECHNICAL APPROACH

The 36 fresh-frozen specimens will be used for this study. All specimens will have weight-bearing radiographs taken prior to surgical treatment to determine the individual HVA, IMA, and DMAA measurements on radiographs. Feet will then be ranked according to magnitude of HVA, stratified into groups of four, and randomly assigned to each of the four procedures. The various osteotomies are the Mitchell, Distal Chevron, Proximal Crescenteric, and Peterson.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

New protocol for FY03.



## DETAIL SUMMARY SHEET

TITLE: Open Versus Arthroscopic Distal Clavicle Resection – A Prospective Randomized Clinical Trial

KEYWORDS:

PRINCIPAL INVESTIGATOR: Doukas, William C., LTC MC  
ASSOCIATES:

DEPARTMENT: Orthopaedics and Rehabilitation  
SERVICE: Orthopedics Surgery

STATUS: N  
INITIAL APPROVAL DATE: 22 April 2003

### STUDY OBJECTIVE

To compare the results obtained performing distal clavicle resections as an open versus arthroscopic procedure. The primary null hypothesis we will be testing is that there is no significant difference in pain relief as measured by Visual Analog Pain scores between closed and open distal clavicle resections. Additionally, we will record and analysis secondary outcomes measures.

### TECHNICAL APPROACH

This is a randomized controlled trial. Two groups will be followed prospectively.

Group 1 – participants treated with an open distal clavicle resection.

Group 2 – participants treated with an arthroscopic distal clavicle resection.

All participants present will be randomly assigned to one of these groups at their enrollment in this protocol. Randomization will be stratified based on three baseline characteristics (gender, etiology of A.C. joint pain, and baseline V.A.S. score).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Prospective, Randomized Controlled Clinical Investigation of MAVERICK™ Total Disc Replacement in Patients with Degenerative Disc Disease

KEYWORDS:

PRINCIPAL INVESTIGATOR: Kuklo, Timothy R., LTC MC  
ASSOCIATES: MAJ Michael Rosner, MC

DEPARTMENT: Orthopaedics and Rehabilitation  
SERVICE: Orthopedics Surgery

STATUS: N  
INITIAL APPROVAL DATE: 26 August 2003

STUDY OBJECTIVE

This study may help to treat medical military beneficiaries who suffer from low back pain.

TECHNICAL APPROACH

This clinical trial has a multi-center, prospective, randomized, controlled design. Patients and surgeons will not be blinded to surgical treatment. The independent radiographic reviewers will not be blinded since they may be able to distinguish between the treatment groups (first group- investigational, second group-control) on the radiographs and/or CT scans.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Prospective Appraisal of Voice in Patients Undergoing Thyroid Surgery – Aerodynamic and Perceptual Sequelae

KEYWORDS:

PRINCIPAL INVESTIGATOR: Solomon, Nancy P., Ph. D. DAC  
ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 21 February 2003

### STUDY OBJECTIVE

To characterize the early and late changes in aerodynamic measures (air pressure and air flow) of voice following thyroid surgery.

To characterize the early and late changes in auditory perceptual measures of voice (judgments of voice quality by experienced clinicians) following thyroid surgery.

To characterize the early and late changes in visual perceptual measures of laryngeal images (judgments of videostroboscopic recordings by experienced clinicians) following thyroid surgery.

### TECHNICAL APPROACH

Candidates for primary thyroid surgery who consent to participate in the partner protocol will have already provided data for the visual-perceptual and auditory-perceptual analyses described herein. They will be informed that those data will be analyzed in greater depth for this portion of the study. Furthermore, they will be informed of the procedures and purposes of the aerodynamic data collection and analysis and offered the opportunity to consent. If they consent to this protocol, only one 15-minute analysis procedure will be added to the overall protocol, which will be conducted at the scheduled pre-operative, and 1-2-week, 3-month, and 6-month post-operative visits.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Hearing Loss and the Perception of Complex Sounds

KEYWORDS:

PRINCIPAL INVESTIGATOR: Leek, Marjorie R., Ph.D., DAC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 21 February 2003  
Umbrella Study

### STUDY OBJECTIVE

To understand the auditory processing of complex sounds like speech in an impaired hearing system, and to determine the mechanisms underlying the detrimental functional effects of sensorineural hearing loss.

### TECHNICAL APPROACH

Eight experiments are described within this NIH proposal. Each one involves prospective data collection from two groups of subjects. The experimental group will be people with sensorineural hearing loss. The control group will consist of subjects with normal hearing. For each of the eight experiments, up to six persons in each subject group will be recruited and studied to secure valid data from at least four subjects in each group. The basic task of the subjects in all experiments is similar to procedures used clinically to evaluate hearing.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Evaluation of an Automatic System for Switching Between Hearing Aid Microphone Modes

KEYWORDS:

PRINCIPAL INVESTIGATOR: Walden, Brian E., Ph.D., DAC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 15 April 2003

### STUDY OBJECTIVE

The purpose of this study is to compare speech recognition, loudness, and subjective preferences for omnidirectional and directional microphone modes in hearing-impaired listeners across a broad range of signal-to-noise ratios (SNRs).

### TECHNICAL APPROACH

This study will compare omni-directional and directional microphone modes programmed into a behind-the-ear (BTE) multiple-memory dual-microphone digital hearing aid (GN ReSound Canta770-D). The two microphone modes, which will be programmed into two memories of the hearing aids in a counterbalanced order, will be compared for speech recognition, subjective preference, and loudness across a broad range of SNRs. The device will be fit binaurally according to the manufacturer's preferred fitting algorithm with full compensation for the normal low-frequency roll-off in the DIR mode. Participants will be instructed that the programs in memories 1 and 2 "process speech differently" with no specific mention of directionality. A push-button in the back of the instruments allows the user to switch between the two memories. The appropriate number of audible tones indicates which memory has been accessed. Participation in this study will require four clinic visits over a four-week period.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Perception of Dissonance by People With Sensorineural Hearing Loss

KEYWORDS:

PRINCIPAL INVESTIGATOR: Tufts, Jennifer, Ph.D., DAC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 6 May 2003

### STUDY OBJECTIVE

To investigate the impact of sensorineural hearing loss on the perception of musical dissonance.

### TECHNICAL APPROACH

This study will consist of two parts. First, measurements of the dissonance of dyads will be made by asking subjects to compare a number of puretone dyads and harmonic complex dyads whose frequency separations will be varied systematically. Second, critical bandwidths will be estimated for each subject through measurements of "auditory filters". This involves measuring thresholds for pure tones in the presence of filtered noise.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Comparison of Two Therapies for Upper Esophageal Sphincter (UES) Dysphagia

KEYWORDS:

PRINCIPAL INVESTIGATOR: Newman, Lisa A., CIV  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Army Audiology & Speech Center

STATUS: N  
INITIAL APPROVAL DATE: 24 June 2003

### STUDY OBJECTIVE

The primary objective is to identify which of two therapy programs results in the largest number of stable, non-oral dysphagic patients who can swallow safely and return to full oral feeding after 6 weeks of intervention.

In addition, our secondary objectives are to:

1. Determine whether patients with residue in the pyriform sinuses who aspirate the residue after the swallow respond better.
2. Define the pathophysiology underlying the swallow dysfunction and those pathophysiologic elements that change as a result of each therapy program.

### TECHNICAL APPROACH

Pharyngeal phase dysphagia can be a severe and costly side effect of stroke and chemoradiation therapy for head and neck cancer, causing the patient to regularly aspirate food and be unable to eat by mouth. A major subset of pharyngeal phase dysphagia is caused by inability to move the bolus completely through the upper esophageal sphincter (UES) during swallowing. Available therapy for this condition is limited and yields a degree of success, but a new therapy procedure, the Shaker exercise, offers an exciting new opportunity to rehabilitate these patients perhaps more effectively and efficiently than the usual therapy program. The 5-year project we are proposing is a randomized, clinical trial of these two therapies in patients with severe pharyngeal phase dysphagia with inability to move the bolus completely through the UES.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Omnidirectional vs. Directional Microphone Performance at Varying Signal-To-Noise Ratios

KEYWORDS:

PRINCIPAL INVESTIGATOR: Walden, Brian E., Dr.

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Army Audiology & Speech Center

INITIAL APPROVAL DATE: 22 July 2003

### STUDY OBJECTIVE

The purpose of this study is to compare speech recognition, loudness, and subjective preferences for omnidirectional and directional microphone modes in hearing-impaired listeners, across a broad range of SNRs.

### TECHNICAL APPROACH

Two groups of hearing-impaired adults – one experienced with switchable omnidirectional/directional hearing aids and the other experienced only with conventional omnidirectional aids – will be recruited. Each participant will be fit binaurally with behind-the-ear (BTE) multiple-memory dual-microphone digital hearing aids. The two microphone modes will be programmed into two memories of the hearing aids. The device will be fit according to the manufacturer's preferred fitting algorithm. Speech recognition will be assessed for the omnidirectional and directional microphone modes across a broad range of SNRs, and the directional advantage (DA) will be computed at each SNR. Subjective preference and loudness comparisons between the two modes will also be assessed at each SNR. The data will be analyzed to determine the relationship between the DA and SNR, and how that function relates to preferences and loudness comparisons between the microphone modes. In addition, acoustic recordings will be made of an artificial speech signal processed through each microphone mode at each SNR using an acoustic manikin. These data will be analyzed to determine if a measure of the amount of speech information transmitted in each microphone mode can predict the DA, as well as the preference and loudness ratings at each SNR.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: Fertility of Men Born by Breech Delivery

KEYWORDS:

PRINCIPAL INVESTIGATOR: Dean, Robert C. LTC MC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: W

SERVICE: Urology

INITIAL APPROVAL DATE:

### STUDY OBJECTIVE

Study withdrawn by PI.

### TECHNICAL APPROACH

Study withdrawn by PI.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn by PI.

### CONCLUSIONS

Study withdrawn by PI.

## DETAIL SUMMARY SHEET

TITLE: Evaluation of A 15-Minute PSA Test For The Detection and Monitoring of Prostate Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Urology

INITIAL APPROVAL DATE: 7 January 2003

### STUDY OBJECTIVE

Determine the concordance in the values obtained for serum total prostate specific antigen (PSA) using a new table-top 15-minute PSA analyzer and PSA obtained by routine laboratory testing at WRAMC in men with prostate cancer, benign prostate conditions, and no prostate disease. Determine the acceptance and satisfaction of patients with the 15-minute PSA test.

### TECHNICAL APPROACH

Men who are being evaluated at CPDR Ward 56 with prostate cancer, with benign prostate conditions, and without known prostate disease will be recruited from those already consenting to the CPDR Serum bank protocol WU# 2801. A consecutive group of 300 men will have blood drawn from which to collect the serum used for analysis by the 15-minute PSA analyzer, and will be asked to complete a questionnaire after informed consent is obtained. They will also have a PSA test sent to the main lab at WRAMC as part of routine patient care. We expect clinically acceptable correlation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

**TITLE:** Mechanical Oral Bowel Preparation For Urinary Diversion Surgery – A Prospective Evaluation of Patients' and Surgeon Satisfaction

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** Jezior, James, LTC MC  
**ASSOCIATES:**

**DEPARTMENT:** Surgery  
**SERVICE:** Urology

**STATUS:** N  
**INITIAL APPROVAL DATE:** 14 January 2003

### STUDY OBJECTIVE

The purpose of this study is to compare patient and physician satisfaction with a preoperative oral bowel preparation using Fleet's Phosphosoda or polyethylene glycol (colyte) prior to urinary diversion surgery using ileal bowel segments. The study will examine the following research question: Are there differences in patient tolerance, physician satisfaction, or electrolyte abnormalities when an oral mechanical bowel preparation using Phosphosoda is used instead of the traditional bowel preparation using polyethylene glycol?

### TECHNICAL APPROACH

Diagnostic Visit	Preoperative Visit	Day Prior to Surgery	Day of Surgery	Post Operatively
Patient identified as needing bowel surgery	Patient completes standard preoperative H&P with primary urologist	Patient may be admitted to hospital (Status will be noted on questionnaires)	1.Pre-op blood chemistry obtained 2.Patient questionnaire completed.	Patient recovers from surgery
1.Study discussion with treating urologist 2.Consent discussion arranged/completed with investigator	1.Preliminary chemistry obtained 2.Complete randomization 3.Final inclusion determined	Bowel preparation administered	1.Urinary diversion or bladder augmentation completed. 2.Surgeon questionnaire completed.	

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Randomized Trial of Radical Prostatectomy Versus Brachytherapy For Patients With T1c or T2a N<sub>0</sub> M<sub>0</sub> Prostate Cancer Protocol Z0070

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC

ASSOCIATES: COL David G. McLeod MC, Caroline Tuman, RN

DEPARTMENT: Surgery

STATUS: N

SERVICE: Urology

INITIAL APPROVAL DATE: 28 January 2003

### STUDY OBJECTIVE

The study objective is to ascertain whether patients assigned to receive brachytherapy have equal or better overall survival as compared to patients randomized to receive radical prostatectomy. Secondary objectives are to compare the two treatment arms with respect to metastasis-free survival, the probability of survival without symptoms, and side effects from intervention. Quality of life is to be addressed in companion study. The companion study will only assess the quality of life of the subjects enrolled in this study.

### TECHNICAL APPROACH

In this study, two different standard of care prostate cancer treatments (brachytherapy vs. prostatectomy) are being compared. Therefore, all procedures done in this protocol are standard of care regardless of what treatment arm the patients are in, except for the submission of samples to the ACOSOG tissue bank, which is being done for research purposes only.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Prostate Cancer Quality of Life Questionnaire

KEYWORDS:

PRINCIPAL INVESTIGATOR: McLeod, David G., COL MC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Urology

INITIAL APPROVAL DATE: 4 February 2003

### STUDY OBJECTIVE

To collect health-related quality of life information on patients newly diagnosed with early stage prostate cancer and to enter it into a Quality of Life Database to be used for subsequent studies.

### TECHNICAL APPROACH

This is a prospective, repeated measures, patient-reported study. It is designed to collect quality of life information from newly diagnosed, early stage prostate cancer patients before the start of cancer treatment (to establish a baseline quality of life) and at fixed intervals after treatment for three years (to measure changes in quality of life over time). The fixed intervals after treatment will be: 3 months, 6 months, 9 months, 12 months, 18 months, 24 months, 30 months, and 36 months. The intervals will, to the extent possible, coincide with the patient's routine follow-up medical appointments. Patients who do not live in the geographical area and/or are unable to travel to WRAMC for follow-up appointments will be mailed the survey instruments and be provided with a postage-paid, pre-addressed return envelope.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Establishment of a Blood-Serum/Plasma Bank from Patients with Prostate Cancer, Benign Prostate Conditions, and Healthy Men – A Master Banking Protocol

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: N  
INITIAL APPROVAL DATE: 11 February 2003

### STUDY OBJECTIVE

The primary goal of this protocol is to establish a blood-serum/plasma bank and to utilize it in developing new technology for the diagnosis, prognosis, and therapeutic responses of prostate cancer patients. Serum/plasma will be obtained from patients with prostate cancer, benign prostate disorders, and no prostate disease/healthy volunteers to use in the evaluation of new markers of disease.

### TECHNICAL APPROACH

This protocol is to renew and expand the existing protocol Work Unit # 2801. All samples collected under 2801 will be carried over to this new protocol. 2801 will be closed upon the approval of this protocol.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Comprehensive Program for the Validation of Prostate Cancer Early Detection with Novel Protein Identification Techniques: Phase I: Synchronization of SELDI Instruments and Validation of Robotic Sample Processing

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC

ASSOCIATES: Amina Ali, BS, MT

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: N

INITIAL APPROVAL DATE: 9 September 2003

### STUDY OBJECTIVE

To validate the use of serum profiling using surface enhanced laser desorption/ionization (SELDI) as an early screening test for detection of prostate cancer in a large multi-institution trial under the Early Detection Research Network (EDRN).

### TECHNICAL APPROACH

The Center For Prostate Disease Research (CPDR) will participate in a large, randomized, double-blinded, multi-center study that aims to validate the clinical utility of serum proteomic profiling using SELDI technology. In Phase I, serum samples from participating institutions will be analyzed using a set serum processing and spectrometric analysis protocol to be followed by all institutions. Bioinformatic analysis on the data will be conducted to develop a classification algorithm/system that will diagnose prostate cancer with great accuracy. Results will be assessed to determine reproducibility and robustness of the classification algorithms across all the participating centers.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Health Related Quality of Life in Patients With Low Risk Localized Prostate Cancer Randomized To Radical Prostatectomy or Brachytherapy Protocol Z0071

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: N  
INITIAL APPROVAL DATE: 11 February 2003

### STUDY OBJECTIVE

The primary objective of this study is to compare changes in health related quality of life (HRQOL) from baseline to up to two years following intervention in patients randomized to undergo either radical prostatectomy or brachytherapy in an American College of Surgeons Oncology Group study, Protocol Z0070. The secondary objectives are to investigate and compare between arms the effect of HRQOL, age, and other covariates on HRQOL changes, over time, during the two year post intervention period, stratified by primary interventions; the effect of primary intervention on HRQOL improvement/deterioration from baseline up to ten years, post-intervention; and the effects of intervention failure as evidenced by cancer progression, on prostate cancer-specific HRQOL (EPIC domains).

### TECHNICAL APPROACH

Patient study information is faxed (not mailed) directly to the DataFax server. The only clinic visit with the sole purpose of answering questionnaires is the month two visit. All other visits for Protocol Z0071 coincide with Protocol Z0070 visits. During these visits, the Z0071 questionnaire should be completed prior to any Z0070 procedures taking place.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: Breast Volume Measurements in Men Receiving Antiandrogen Treatment For Rising PSA

KEYWORDS:

PRINCIPAL INVESTIGATOR: McLeod, David G., COL MC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Urology

INITIAL APPROVAL DATE: 25 February 2003

### STUDY OBJECTIVE

The primary objective of this study is to document breast volume measurements in men receiving antiandrogen monotherapy for rising PSA. The secondary objectives are:

- Evaluate breast measurements in patients receiving adjuvant radiation therapy prior to the start of antiandrogen monotherapy to that of men who did not select adjuvant radiation therapy.
- Evaluate relationship of breast tenderness to treatment choice and length of time on hormonal therapy.

### TECHNICAL APPROACH

This is a pilot study. Men will have 3-D photographic images taken of their breasts a total of five times, complete a breast tenderness visual analog scale five times, and have their PSA and testosterone levels drawn five times during the course of the study. The patient's face will not appear in any of the photographs. The breast photographs and tenderness scale are for research purposes while the blood work is standard of care for men receiving hormonal therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Randomized, Double-Blind, Placebo Controlled Trial of Immunotherapy With Autologous Antigen-Loaded Dendritic Cells (Provenge™) for Asymptomatic Metastatic Hormone-Refractory Prostate Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: McLeod, David G., COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: N  
INITIAL APPROVAL DATE: 25 February 2003

### STUDY OBJECTIVE

The study may produce information regarding the progression, treatment, and/or prevention of prostate cancer in the Military Health Systems beneficiary population.

### TECHNICAL APPROACH

Up to 10 male military health care beneficiaries from Walter Reed Army Medical Center will enroll in this study. Overall, about 120 men will take part in this study. The study will be conducted at multiple oncology care institutions nationwide. There will be 3 to 5 Dendreon designated cell-processing centers. This is a prospective Phase III, double blind, placebo controlled, randomized trial of immunotherapy with autologous antigen-loaded dendritic cells for the treatment of asymptomatic metastatic hormone-refractory prostate cancer patients.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

**TITLE:** A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study of the Efficacy and Safety of Dutasteride 0.5mg Administered Once Daily For Four Years to Reduce The Risk of Biopsy-Detectable Prostate Cancer

**KEYWORDS:**

**PRINCIPAL INVESTIGATOR:** McLeod, David G., COL MC  
**ASSOCIATES:**

**DEPARTMENT:** Surgery  
**SERVICE:** Urology

**STATUS:** N  
**INITIAL APPROVAL DATE:** 25 March 2003

### STUDY OBJECTIVE

**Primary:** To assess the effect of repeat oral dose once daily dosing of 0.5mg dutasteride compared to placebo on the risk of biopsy-detectable carcinoma of the prostate after two years and four years of treatment.

**Secondary:** To assess safety and tolerability of 0.5mg dutasteride compared to placebo. To assess clinical and histopathological effects of 0.5mg dutasteride compared to placebo. To assess the effect of 0.5mg dutasteride compared to placebo on the symptoms of benign prostatic hyperplasia (BPH). To assess the effects of 0.5mg dutasteride compared to placebo on serum testosterone (T), dihydrotestosterone (DHT), and free and total prostate specific antigen (PSA). To assess the effects of 0.5mg dutasteride compared to placebo on health outcome measures.

### TECHNICAL APPROACH

All study participants will undergo TRUS and prostate biopsy at two years and four years post randomization. In addition, a TRUS will be performed at baseline for determination of prostate volume, unless this has been performed within the previous six months. Blood samples for the analysis of serum/plasma proteins will be collected at screening visit one and at each six-month clinic visit thereafter. Samples will be collected and shipped according to guidelines provided by GSK or the central laboratory. The effect of dutasteride on health related quality of life will be assessed using five self-administered questionnaires. The International Prostate Symptom Score (IPSS) is the primary questionnaire-based study endpoint. All subjects will be assigned to a single blind, four-week placebo run-in period prior to randomization. Once the placebo run-in period has been completed, eligible subjects will be assigned to study treatment in accordance with the randomization schedule.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Urine Protein Patterns as Potential Diagnostic Biomarker For Urolithiasis

KEYWORDS:

PRINCIPAL INVESTIGATOR: Brassell, Stephen A., CPT MC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Urology

INITIAL APPROVAL DATE: 1 April 2003

### STUDY OBJECTIVE

ProteinChip surface enhanced laser desorption/ionization (SELDI) mass spectrometry is a newly developed technology which is able to rapidly analyze protein expression patterns in serum or urine that could be linked to a specific disease. Like cDNA microarray to assess mRNA expression, proteomics analyze the complexity of protein expression in a given biologic system. We propose to use to Ciphergen proteomics technology to study the urine of patients afflicted with stone disease. Our objective is to develop a protein fingerprint that is indicative of stone formers.

### TECHNICAL APPROACH

Because of the distinct difference in rates of urolithiasis between males and females with an approximate 3:1 male to female ratio, there will be four test groups: male stone formers, female stone formers, male controls, and female controls. The full analysis will include fifty subjects from each group. However, due to the exploratory nature of this study, initial testing of a smaller sample size (20 in each group for a total of 80 samples) will be done. If testing of these first 80 samples does not show a specificity of  $\geq 80\%$ , the study will be stopped. The protein spectra from the training set samples will be analyzed by biomarker recognition software purchased from a commercial source. A proteomic pattern will be created to discriminate stone forming patients from control individuals. Future studies may entail applying these templates to a generalized population in a prospective evaluation in order to determine the validity of these characterizations.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Phase II, Open Label, Single Arm Trial With Cryopreserved Autologous Antigen-Loaded Dendritic Cells (Provenge™), APC8015F For Hormone-Refractory Prostate Cancer Patients With Objective Disease Progression – Protocol D9903

KEYWORDS:

PRINCIPAL INVESTIGATOR: McLeod, David G., COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: N  
INITIAL APPROVAL DATE: 8 April 2003

### STUDY OBJECTIVE

The study may produce information regarding the progression, treatment, and/or prevention of prostate cancer in the Military Health Systems beneficiary population.

### TECHNICAL APPROACH

This is a Phase II open label salvage trial for control patients enrolled in Dendreon's Phase III protocols D9901 and D9902. Patients who were randomized to placebo in Dendreon's Phase II trial of APC8015, Protocol D9901 or D9902, and who develop objective disease progression will be considered for the salvage protocol. Additional eligibility criteria include ECOG performance status of  $\leq 2$ , adequate hematological, renal and liver functions (WBC  $\geq 2,000$ ; ANC  $\geq 1,000$ ; Platelet count  $\geq 100,000$ ; HgB  $\geq 9$  gm/dL; creatinine  $\leq 2 \times$  ULN; AST, ALT  $\leq 5 \times$  ULN), and a life expectancy of at least 16 weeks.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Phase IIb, Multi-Center, Randomized, Double-Blind, Placebo-Controlled Trial to Assess the Safety and Efficacy of MPC-7869 in Delaying the Systemic Progression of Prostate Cancer in Patients With Intermediate to High Risk of Recurrence With Rising Prostate Specific Antigen (PSA) Levels

KEYWORDS:

PRINCIPAL INVESTIGATOR: McLeod, David G., COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: N  
INITIAL APPROVAL DATE: 22 April 2003

### STUDY OBJECTIVE

This study is being done to determine if MPC-7869 will be useful to men with prostate cancer who, after surgical removal of the prostate, surgical removal of the prostate along with radiation therapy, or radiation therapy alone, have rising serum PSA (prostate specific antigen) levels.

### TECHNICAL APPROACH

This is a multicenter, randomized, double blind, and placebo-controlled, 36-month trial with a 12-month enrollment period. Approximately 390 prostate cancer patients, age 18 years or older, at intermediate to high risk for prostate cancer recurrence are eligible for inclusion.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: An Open Label, Single Arm Trial of Immunotherapy with Autologous Antigen Presenting Cells Loaded with PA2021 (APC8015F) for Subjects with Objective Disease Progression and Disease-Related Pain on Protocol D9902 Part B

### KEYWORDS:

PRINCIPAL INVESTIGATOR: COL David G. McLeod, MC

ASSOCIATES: Thomas Esther, PA, COL Judd W. Moul, MC, Kimberly Peay, ANP, Kathy Sanetrik, RN

DEPARTMENT:

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 16 September 2003

### STUDY OBJECTIVE

The purpose of this study is to evaluate APC8015F as a treatment for prostate cancer. This is a multicenter, open label, single arm trial. Subjects will be evaluated for eligibility criteria and receive APC8015F at Weeks 0, 2, and 4. Subjects will be evaluated at baseline, Weeks 8, 16, and 24 for the safety and efficacy measurements.

### TECHNICAL APPROACH

This is a Phase II open label salvage trial for control patients enrolled in Dendreon's Phase II protocol D9902B. Patients who were randomized to placebo in Dendreon's Phase II trial of the D9902B, and who develop objective disease progression, will be considered for this salvage protocol.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Study of the Efficacy and Safety of the Mentor Soft-Solid Testicular Prosthesis (SSTP)

KEYWORDS:

PRINCIPAL INVESTIGATOR: McLeod, David G., COL MC

ASSOCIATES: Gary Blake, CRC, Greg Bernstein, MC

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: N

INITIAL APPROVAL DATE: 30 September 2003

### STUDY OBJECTIVE

The purpose of this protocol is to study Mentor's Soft-Solid Testicular Prosthesis (SSTP) via an Investigational Device (IDE).

### TECHNICAL APPROACH

This is a multicenter, non-masked study with up to 10 investigation sites and a total of up to 60 patients enrolled. Patients will be followed for 12 months postoperatively.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: Benign Glands at the Margin of Radical Prostatectomy Specimens – Is This T2 or T3 Disease?

KEYWORDS:

PRINCIPAL INVESTIGATOR: Koff, Stacey, CPT MC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Urology

INITIAL APPROVAL DATE: 18 March 2003

### STUDY OBJECTIVE

The main objective of this study is to determine if patients who have benign glands at the margin of their radical prostatectomy specimen have outcomes that are similar to patients with T2 (organ confined) or patients with T3 (extracapsular) prostate cancer. An additional objective would be to ascertain the frequency of this occurrence and what risks are associated with it. Another objective is to compare the PSA level of those patients with benign glands to those with extracapsular extension, positive surgical margins and negative surgical margins.

### TECHNICAL APPROACH

This is a retrospective chart review of subjects consented under WU# 2857-98 to see if the clinical course and PSA values of men with benign glands at their surgical margin differs from men without benign glands at their surgical margin. Specific variables include clinical stage at diagnosis, surgical approach, pathologic findings (all independent variables), PSA on follow-up visits, and evidence of biochemical or clinical recurrence (outcome variables).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: PSA Density, PSA Velocity, and Free PSA as Predictors of Tumor Volume, Pathologic Stage, and Recurrence

KEYWORDS:

PRINCIPAL INVESTIGATOR: Brassell, Stephen A., CPT MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: N  
INITIAL APPROVAL DATE: 18 March 2003

### STUDY OBJECTIVE

To determine if PSA density (PSAD), PSA Velocity (PSAV), and Percent Free PSA (%FPSA) can serve as better prognosticators than PSA alone in determining pathologic characteristics and biochemical recurrence of prostate cancer.

### TECHNICAL APPROACH

This is a retrospective study spanning 1 January 1990 to 31 December 2002. It will consist of querying the CPDR database for patients diagnosed with prostate cancer and subsequently undergoing radical prostatectomy during this time frame while meeting the inclusion and exclusion criteria. Our goal is to determine which indicator provides a more accurate determination of the tumor volume, extracapsular extension, margin status, and biochemical recurrence than total PSA itself. This may allow for more precise preoperative staging and counseling of prostate cancer patients.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: The Influence of Obesity of Perioperative and Postoperative Morbidity Associated With Radical Prostatectomy

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: N  
INITIAL APPROVAL DATE: 6 May 2003

### STUDY OBJECTIVE

Determine if increased body mass index (BMI) is associated with longer operative times, greater blood loss, and need for blood transfusion in men undergoing radical prostatectomy. Investigate whether men with increased BMI have a higher incidence of early (within 30 days) or late post-operative complications after radical prostatectomy.

### TECHNICAL APPROACH

This is a retrospective study. The only demographic data that will be collected is race and age at surgery. The data will be emailed to PI at Naval Medical Center. We have previously reported an association between obesity and more aggressive (later stage, higher grade) disease. But, for the present study, although these factors will be compared to verify equality between groups, the relationship between these factors (grade, stage, PSA, etc.) and obesity will not be assessed.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Relationship Between Prior Vasectomy and the Incidence and Clinical Characteristics of Prostate Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: N  
INITIAL APPROVAL DATE: 6 May 2003

### STUDY OBJECTIVE

Determine if prior vasectomy increases the risk of finding prostate cancer in men referred for prostate biopsy. Compare clinical and pathologic features of prostate cancer between men with and without a history of prior vasectomy to determine if vasectomy history is associated with more advanced prostate cancer at the time of radical prostatectomy.

### TECHNICAL APPROACH

Up to 5,000 military health care beneficiaries age 18 years and older presenting between 1980 and 2002 referred for initial prostate biopsy, whether biopsy was positive or negative, and those undergoing radical prostatectomy over this time period will be studied.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Multicenter Retrospective Review of the Use of Watchful Waiting in An Equal-Access Health Care System

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Urology

STATUS: N  
INITIAL APPROVAL DATE: 6 May 2003

### STUDY OBJECTIVE

The goal of this study is to conduct a thorough analysis and comparison of the use of watchful waiting as a primary treatment option for patients with prostate cancer and to observe trends regarding race, severity of disease, and mortality. The purpose of this project is to help determine which population of patients, both pathologically and demographically, is best suited for watchful waiting.

### TECHNICAL APPROACH

This is a retrospective study. The following two predictor variables will be added for this protocol: family history of prostate cancer and percentage of positive biopsy samples.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Integration of Biomarkers and Clinical Factors for Early Detection of Metastatic Prostate Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Moul, Judd W., COL MC

ASSOCIATES: Holly Wu, MD

DEPARTMENT: Surgery

SERVICE: Urology

STATUS: N

INITIAL APPROVAL DATE: 22 July 2003

### STUDY OBJECTIVE

The objective of this proposal is to develop an early Metastatic Prostate Cancer (MPC) detection system implemented in a web application for physicians' decision making and patients' self-assessment. In this proposal, we plan to use three approaches to establish the early MPC detection system: (1) Understand the molecular biological mechanism of MPC by characterizing the gene expression profiles of the above biomarkers and their role in MPC, (2) Study the clinical factors in different clinical scenarios and their association with MPC, and (3) Integrate the findings from the molecular biology and clinical studies by using mathematical and statistical data mining techniques. The hypothesis is that MPC is a complicated event linked with multiple intrinsic gene expression changes and affected by clinical factors. The proposal is based on our previous study on *NKX3.1*, *PMEPAI* and *PSGR* from same group of PC patients and the following unique resources: (1) The CPDR Tissue Bank that contains more than 800 radical prostatectomy specimens and about 150 new cases annually, and (2) The CPDR National Database, which maintains more than 450,000 longitudinal clinical records on 18,000 men, including all the men in the CPDR Tissue Bank.

### TECHNICAL APPROACH

We propose to accomplish our objective by first characterizing the tumor burden and gene expression profiles of *NKX3.1*, *PMEPAI* and *PSGR* and their association with MPC. Then we will clarify the role of the multiple clinical factors and their interactions on MPC. The findings from the study on biomarkers and clinical factors will be integrated by using the traditional and popular data mining methods (neural networks and decision tree) and expressed in algorithms and nomograms. With a validation data set and the prospectively collected data, these algorithms and nomograms will be tested, validated, and improved for the probability of early MPC detection. The validated algorithms and nomograms will be implemented into a web application accessible through the Internet.

This study's product, Early MPC Detection System, is likely a practical solution to the key problem in control of prostate cancer progression and mortality. The concept and approaches are novel, logical, and practical, which may impact the design of novel diagnostic approaches in other cancers.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Efficacy and Safety of Drotrecogin Alfa (Activated) in Adult Patients With Early Stage Severe Sepsis (Protocol F1K-MC-EVCL, Eli Lilly and Co.)

KEYWORDS:

PRINCIPAL INVESTIGATOR: Jackson, William L., MAJ MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Critical Care Medicine

STATUS: N  
INITIAL APPROVAL DATE: 10 June 2003

### STUDY OBJECTIVE

This is an extramural study that is part of a Master Protocol (Protocol F1K-MC-EVCL, Eli Lilly and Company). Please see page 10 of the Master Protocol.

### TECHNICAL APPROACH

This study will be conducted using the drug drotrecogin alfa (activated), which has been approved by the FDA for the treatment of severe sepsis in patients at high risk of death (as determined, for example, by the Acute Physiology and Chronic Health Evaluation [APACHE II] severity-of-illness scoring system). However, the use of this drug for the treatment of early stage severe sepsis is still investigational (experimental) and has the IND # BB-IND-5919 which is held by Eli Lilly and Company. A copy of the Investigators Brochure is on file in the Research Review Service, Department of Clinical Investigation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Prospective, Randomized, Double-Blinded Comparison Study of Coblation and Coherent Ultra Pulse CO2 Laser Skin Resurfacing Therapies

KEYWORDS:

PRINCIPAL INVESTIGATOR: Winslow, Catherine P., MAJ MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Otolaryngology – Head & Neck

STATUS: N  
INITIAL APPROVAL DATE: 22 October 2002

### STUDY OBJECTIVE

Compare the efficacy and degree of morbidity of Coblation and Coherent Ultra Pulse Carbon Dioxide Laser skin resurfacing therapies. Specifically, we will quantify the degree of post-operative morbidity to include pain, erythema, and edema to determine if Coblation therapy has a significant reduction in post-operative morbidity when compared to the Carbon Dioxide Laser therapy. Hypothesis is that while Coblation therapy may prove to have a statistically significant reduction in post-operative morbidity and a shorter time to complete re-epithelialization, it may not provide the desired clinical efficacy that Carbon Dioxide Laser therapy has shown.

### TECHNICAL APPROACH

Methodology includes a pre-operative assessment, a facial analysis using Glogau's Classification of Photoaging Groups, photography, randomization, pre-operative skin care regimen/HSV prophylaxis, anesthesia, surgery, post operative skin care regimen/infection prophylaxis, and post operative follow-up. At the six-month end point, we expect that all pain, edema, erythema, and rhytid reduction will be achieved.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: Gene Expression Analysis in Sinonasal Polyposis and Anosmia

KEYWORDS:

PRINCIPAL INVESTIGATOR: Bolger, William E., MD DAC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Otolaryngology – Head & Neck

INITIAL APPROVAL DATE: 25 February 2003

### STUDY OBJECTIVE

Explore the gene expression change in nasal polyps following oral methylprednisolone treatment (immediate objective).

Identify the major human signal transduction pathways that are active in the ameliorative response of oral methylprednisolone in nasal polyps (long-term objective).

### TECHNICAL APPROACH

Day 0	Day 1	Day 28 Intervention	Day 90
1. Patient recruitment 2. Screen for inclusion and exclusion criteria 3. Informed consent 4. Olfactory test - "scratch & sniff" 5. Nasal endoscopy 6. Endoscopic minimally invasive biopsy	Begin methylprednisolone: - Every morning for 7 days. - Then every other morning for 20 days. (A tapering and alternate day regimen)  Monitor for adverse effects	1. Olfactory test - "scratch and sniff" 2. Nasal endoscopy 3. Endoscopic minimally invasive biopsy	Routine follow-up exam

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Physiology and Safety Profile of Radio-Frequency Ablation of Thyroid Tissue in Pigs (*Sus scrofa domestica*)

KEYWORDS:

PRINCIPAL INVESTIGATOR: Melder, Patrick C., MAJ MC  
ASSOCIATES:

DEPARTMENT: Surgery  
SERVICE: Otolaryngology – Head & Neck

STATUS: N  
INITIAL APPROVAL DATE: 18 March 2003

### STUDY OBJECTIVE

Primary Objective: Determine if radio-frequency energy can be used to produce volumetric reduction of normal thyroid tissue.

Secondary Objectives:

1. Evaluate the safety of RFA in the thyroid gland both from the standpoint of its direct physical effects (e.g., potential for injury to neighboring anatomic structures) and its secondary physiologic effects (e.g., potential for follicular-cell release of thyroid hormone in response to radio-frequency-energy-induced injury).
2. Assess the effect of radio-frequency energy on thyroid tissue over four different doses of RFA.
3. Describe the histologic characteristics of radio frequency ablated thyroid tissue.

### TECHNICAL APPROACH

The primary endpoint for this protocol is stabilization of thyroid volume following radio-frequency ablation. Secondary endpoints include normalization of serum thyroid hormone levels. Animals will be survived for six weeks or until the above endpoints are reached, whichever comes first. Euthanasia will be performed following total thyroidectomy (while the animals are still anesthetized) once the endpoints are reached.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: EndoCDx – Evaluation of Pharyngeal and Laryngeal Lesions With Computer-Assisted Analysis or Brush Biopsy Specimens

KEYWORDS:

PRINCIPAL INVESTIGATOR: Battiata, Andrew, CPT MC  
ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Otolaryngology-Head & Neck Surgery

INITIAL APPROVAL DATE: 13 May 2003

### STUDY OBJECTIVE

Up to 60 military health care beneficiaries age 18 years and older presenting abnormal lesions in the pharynx and larynx will be evaluated. This is a multi-center study in which a total of approximately 650 patients will be enrolled at approximately 20 different sites.

### TECHNICAL APPROACH

Suspicious lesions will undergo biopsy in the standard fashion. Prior to biopsy, however, a scraping of the surface cells will be obtained in the clinic, utilizing the brush biopsy technique and analyzed for evidence of dysplasia. Additionally, lesions that would not have otherwise been biopsied (i.e. would have been followed clinically) will be sampled by a brush biopsy (scraping the surface cells) and analyzed. This has the benefit of potentially diagnosing dysplasia or carcinoma earlier than with the current standard of care, and hopefully improving outcomes.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Detection of Pre-cancerous and Cancerous Lesions of the Oropharynx With OpCDx (Computer Assisted Analysis of Brush Biopsy Specimens) – A Multicenter Prospective Clinical Trial

KEYWORDS:

PRINCIPAL INVESTIGATOR: Battiatà, Andrew, CPT MC  
ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Otolaryngology-Head & Neck Surgery

INITIAL APPROVAL DATE: 13 May 2003

### STUDY OBJECTIVE

Potentially diagnosing dysplasia or carcinoma earlier than with the current standard of care.

### TECHNICAL APPROACH

Biopsies will be taken of lesions of the oropharynx, which is bounded by the soft palate superiorly, anterior tonsillar arches anteriorly (palatoglossus muscles) inferiorly by the approximate level of the hyoid bone, and posteriorly by the posterior pharyngeal wall.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Utility of Cytoscan Model E-II for Intraoperative Parathyroid Gland Identification – A Pilot Study

KEYWORDS:

PRINCIPAL INVESTIGATOR: LT Michael A. Hoffmann, MC, USNR

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Otolaryngology-Head & Neck Surgery

INITIAL APPROVAL DATE: 29 July 2003

### STUDY OBJECTIVE

The study is designed to test the suitability of the Cytoscan Model E-II utilizing Orthogonal Polarization Spectral (OPS) imaging in the intra-operative identification of parathyroid tissue, thyroid tissue, and adipose tissue.

### TECHNICAL APPROACH

Research design: Prospective.

Methodology: Obtain intra-operative images of parathyroid, thyroid, and adipose tissue using the Cytoscan Model E-II in twelve patients that have been previously consented for the study and meet indications for procedures involving biopsy of the previously stated tissues. The identity of the tissues imaged will be confirmed by the surgically indicated biopsies. The images will then be randomly presented to four blinded otolaryngologists for proper identification.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Characterization of Human Olfactory Ensheathing Cells *in Vitro*

KEYWORDS:

PRINCIPAL INVESTIGATOR: Bolger, William E., MD DAC

ASSOCIATES:

DEPARTMENT: Surgery

STATUS: N

SERVICE: Otolaryngology-Head & Neck

INITIAL APPROVAL DATE: 9 September 2003

### STUDY OBJECTIVE

The long-term goal of this project is to development of a method to isolate and propagate human olfactory ensheathing cells (OECs) for transplantation to enhance spinal cord regeneration and functional recovery. To reach this goal, it is necessary to fully characterize human OECs *in vitro* and study their properties after transplantation in animal models of SCI before use in humans.

### TECHNICAL APPROACH

This study will: (1) establish purified human OECs in primary culture, (2) identify neurotrophic factors expressed, translated, and secreted by human OECs *in vitro*, (3) identify mitogenic factors that promote proliferation of human OECs *in vitro*, and (4) investigate migration capacity of human OECs subjected to different growth factors and extracellular matrix molecules.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Oropharyngeal Vaccinia Virus Presence After Smallpox Vaccination

KEYWORDS:

PRINCIPAL INVESTIGATOR: Klote, Mary M., CPT MC

ASSOCIATES:

DEPARTMENT: Allergy-Immunology

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 3 December 2002

### STUDY OBJECTIVE

To identify if vaccinia virus is present in the pharyngeal mucosa after vaccination with smallpox vaccine. To identify if there is a difference in incidence of viral presence between new vaccinees and those who have been vaccinated previously. If virus is present, to see if there is a correlation between signs and symptoms and time virus is found.

### TECHNICAL APPROACH

All vaccine recipients must report for bandage change prior to reporting to work each day they work in the hospital. This is required by the hospital, not the research study. Collection of our samples will occur in parallel with the days the soldiers will be coming for bandage change. However, if they are not scheduled to work on one of those days, they will be asked to come in to have a throat culture done. Swabbing will occur prior to bandage change and the two will not be directly co-located. All vaccine recipients complete a symptom diary for the thirty days following vaccination. Any participant experiencing concerning reactions or more serious reactions to the vaccine will be referred to the Vaccine Healthcare Center at WRAMC. Specimens will be sent to USAMRIID's research lab for processing and identification of vaccinia virus. After identification, the samples will be destroyed.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Immune Responses to Smallpox Vaccination

KEYWORDS:

PRINCIPAL INVESTIGATOR: Nelson, Michael R., LTC MC  
ASSOCIATES:

DEPARTMENT: Allergy-Immunology  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 10 December 2002

### STUDY OBJECTIVE

Measure the dominant cytokine response profiles, neutralizing antibody titer, and inflammatory response parameters in smallpox vaccine recipients during the first thirty days following immunization. As a pilot study, establish a serum bank for future research regarding the immune and inflammatory response parameters during the first thirty days following smallpox vaccination.

### TECHNICAL APPROACH

This is a prospective pilot cohort study investigating the patterns of immune responses to smallpox vaccine in the first thirty days following immunization with a licensed calf-lymph derived vaccine (Dryvax) until resolution of vaccine response symptoms and loss of scab (end point for successful immunization). The diary to be used at WRAMC as part of the smallpox immunization program is an adaptation of the DOD symptom diary and a questionnaire used during the first phase of immunizations performed through the Clinical Immunization Safety (CISA) network. Participants who are revaccinated on days 6-8 after initial vaccination (per standard of care) because no pustule has formed will have their "clock" reset to day zero and a new diary begun on that day. Blood specimens will be collected to capture the peak and resolved phase of a vaccinia response. Blood will be processed by the WRAMC Department of Pathology. Processing includes immunological assays, enumeration of T cell numbers by flow cytometry, proliferation in response to vaccinia virus, cytokine production in response to vaccinia virus, and production of neutralizing antibodies to vaccinia.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: Cell Mediated Immune Response to Anthrax Vaccination

KEYWORDS:

PRINCIPAL INVESTIGATOR: Klote, Mary M., CPT MC

ASSOCIATES:

DEPARTMENT: Allergy-Immunology

SERVICE:

STATUS: N

INITIAL APPROVAL DATE: 20 May 2003

### STUDY OBJECTIVE

Measure the cell-mediated immune (CMI) response in participants formerly vaccinated with the anthrax vaccine. Develop immunologic assays for examining reactivity to recombinant Protective Antigen (rPA).

### TECHNICAL APPROACH

This is a prospective pilot study investigating the induction and memory of CD4+ T cells after vaccination with the anthrax vaccine and seeing how well this response correlates with antibody response. Thus, in all individuals, the anti-PA IgG titer will be assessed. We will examine the CD4 T cell response through novel cell-based assays for detection of prior anthrax vaccination. Prospective participants will be within five years of having had at least two documented AVA vaccinations. Variables we will consider include age, gender, prior vaccination status, dates of vaccination with anthrax, other vaccinations received on same day as anthrax vaccination (if available), current medications, and medical problems.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Comparison of Skin Test Devices for Prick Testing.

KEYWORDS:

PRINCIPAL INVESTIGATOR: MAJ Warner W. Carr MC

ASSOCIATES: COL Bryan Martin MC, Clarence Yarborough, Levi Harvey

DEPARTMENT: Allergy and Immunology

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 26 August 2003

### STUDY OBJECTIVE

To determine the differences in the size of wheal and flare reactions for both positive (histamine) and negative (glycerol-saline) sites between various skin testing devices.

To determine the differences in patient discomfort experienced with different skin test devices.

### TECHNICAL APPROACH

The purpose of this study is to compare the performance of various FDA approved skin test devices in a prospective blinded fashion. The study is a prospective, blinded study. In a blinded fashion, and using standard techniques, one technician will apply skin tests with either histamine or saline. Another technician, blinded to which device was used, will record the results. In order to control for variations in response based on anatomic site, each device will be evaluated on the standard arm and back sites. Each patient will be given a standardized pain scale to complete during each testing session.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Emergency Use Protocol For the Administration of Vaccinia Immune Globulin (Human) To Subjects Who Experience Complications Resulting From Vaccination With Vaccinia Virus

KEYWORDS:

PRINCIPAL INVESTIGATOR: Hack, Dallas C., COL MC  
ASSOCIATES:

DEPARTMENT: Preventive Medicine  
SERVICE:

STATUS: W  
INITIAL APPROVAL DATE: 10 December 2002

### STUDY OBJECTIVE

Study withdrawn.

### TECHNICAL APPROACH

The drug to be used in this study, Vaccinia Immune Globulin (Human), is investigational and will be used under IND number BB-IND 8429, which is held by Centers for Disease Control. To be studied are any active duty subjects with complications resulting from the administration of Vaccinia Virus vaccine. Blood and urine samples will be discarded when the requested clinical testing has been completed. Subjects in this study will be admitted to the Medicine Wards and Intensive Care (Medicine) as their basic medical condition warrants.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn.

### CONCLUSIONS

Study withdrawn.

## DETAIL SUMMARY SHEET

TITLE: Hydroxychloroquine in the Treatment of Erosive Osteoarthritis

KEYWORDS:

PRINCIPAL INVESTIGATOR: Delaney, Nancy, LCDR MC

ASSOCIATES:

DEPARTMENT: Medicine

STATUS: W

SERVICE: Rheumatology

INITIAL APPROVAL DATE: 20 February 2003

### STUDY OBJECTIVE

Study withdrawn.

### TECHNICAL APPROACH

Study withdrawn.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

Study withdrawn.

### CONCLUSIONS

Study withdrawn.

## DETAIL SUMMARY SHEET

TITLE: Lymphocyte Signaling Defects in Patients With Lupus

KEYWORDS:

PRINCIPAL INVESTIGATOR: Mitchell, Jeanne P., MAJ MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Rheumatology

STATUS: N  
INITIAL APPROVAL DATE: 22 April 2003

### STUDY OBJECTIVE

1. Define the mechanisms that are involved in the decreased expression of  $\zeta$ chain in SLE patients.
  - a. Define the role of defective expression of the TCR  $\zeta$ chain enhancer Elf-1 in the decreased expression of  $\zeta$ chain.
  - b. Define the role of the repressor CREM in the suppression of  $\zeta$ chain gene transcription.
  - c. Study the TCR  $\zeta$ chain mRNA stability in SLE T cells.
  - d. Define the extent to which ubiquitination contributes to the degradation of  $\zeta$ chain in SLE T cells.
2. Study the composition and kinetics of rafts on the surface membrane of SLE T cells.
3. Characterize the transcriptional requirements for the increased expression of Fc $\gamma$  chain.

### TECHNICAL APPROACH

These experiments are expected to provide a cross-sectional analysis of the white blood cell (T cells) signaling aberrations with lupus disease activity. For all of the experiments, three groups of patients will be identified as follows: lupus patients, normal controls, disease controls. We also plan to perform a prospective analysis of the lupus patients. All lupus study subjects will be followed for two years after their initial clinical evaluation. The frequency of their follow-up will be determined by their disease activity but will occur annually, at a minimum. All lupus subjects will have a blood sample at the time of enrollment.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Pre-Clinical Autoimmunity in Rheumatoid Arthritis

KEYWORDS:

PRINCIPAL INVESTIGATOR: Gilliland, William, LTC MC  
ASSOCIATES:

DEPARTMENT: Medicine  
SERVICE: Rheumatology

STATUS: N  
INITIAL APPROVAL DATE: 22 April 2003

### STUDY OBJECTIVE

To identify health individuals during the pre-clinical phase of disease who are at sufficiently high risk for developing rheumatoid arthritis (RA) so that a primary prevention strategy can be developed in the future.

### TECHNICAL APPROACH

This study is a retrospective evaluation for the presence of RA-related autoantibodies in pre-disease serum samples of patients with RA. Because subjects with hepatitis C have a higher rate of rheumatoid factor positivity than the general population, the most recent serum samples from both cases and controls will be tested for anti-hepatitis C antibodies in order to exclude any subjects with hepatitis C not previously diagnosed.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Prevention of Perioperative Thromboembolism in Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Maxwell, G. Larry, MAJ MC

ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 4 April 2003

### STUDY OBJECTIVE

Aim 1: Compare external pneumatic compression to external pneumatic compression plus low molecular weight heparin for the perioperative prophylaxis of patients at high risk for thromboembolism despite single agent prophylaxis (2 of the 3 following criteria: history of DVT, diagnosis of cancer, age >60 years).

Aim 2: Identify preoperative screening tests that could be predictive of perioperative thromboembolism despite single agent or combination prophylaxis.

### TECHNICAL APPROACH

Up to 300 female military health care beneficiaries presenting to the Walter Reed Army Medical Center (WRAMC) Department of OB/GYN, Division of GYN Oncology who will undergo major abdominal or pelvic surgery for known or presumed gynecologic malignancy. A total of up to 1,524 patients, age 18 or older will be enrolled at the 20 sites participating in the Gynecologic Oncology Group sponsored trial.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: GOG #0201, Treatment of Patients With Stage IB2 Carcinoma of the Cervix - A Randomized Comparison of Radical Hysterectomy and Tailored Chemo-Radiation vs. Primary Chemo-Radiation

KEYWORDS:

PRINCIPAL INVESTIGATOR: LCDR John C. Elkas, MC, USN  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: N  
INITIAL APPROVAL DATE: 15 July 2003

### STUDY OBJECTIVE

The objectives of the primary protocol are:

1. To compare progression-free survival and survival of patients having radical hysterectomy followed by tailored chemo-radiation to primary chemo-radiation in the management of patients with Stage IB2 (>4 cm) cervical cancer.
2. To compare the toxicity of combined therapy (surgery + tailored chemo-radiation to primary chemo-radiation in patients with Stage IB2 (>4 cm) cervical cancer.
3. To compare health-related quality of life in-patients managed by combined therapy (surgery + tailored chemo-radiation) to primary chemo-radiation in-patients with Stage IB2 cervical cancer.

### TECHNICAL APPROACH

This is a phase III randomized study of radical hysterectomy and tailored chemo-radiation versus primary chemo-radiation in patients with Stage IB2 carcinoma of the cervix. After meeting eligibility requirements, patients will be randomized to one of two treatment arms. They will receive either chemo-radiation alone, or will undergo a radical hysterectomy and chemo-radiation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: GOG 0195 – A Phase III Clinical Trial of Tisseel® VH Fibrin Sealant to Reduce Lymphedema Incidence after Inguinal Lymph Node Dissection Performed in the Management of Vulvar Malignancies

KEYWORDS:

PRINCIPAL INVESTIGATOR: Elkas, John Christopher, LCDR, MC, USN  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: N  
INITIAL APPROVAL DATE: 30 September 2003

STUDY OBJECTIVE

This study is being done to determine if vulvar cancer patients who have a vulvectomy concurrent with inguinal lymphadenectomy may also benefit from the use of fibrin sealant in the groin wound.

TECHNICAL APPROACH

The fibrin sealant may reduce the incidence of lymphedema and wound complication thereby improving the comfort of the patient.

PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: GOG 0190 – An Exploratory Evaluation of Fenretinide (4-HPR) (IND #39,812) as a Chemopreventive Agent for Ovarian Carcinoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Elkas, John Christopher, LCDR  
ASSOCIATES: LTC G. Scott Rose, MC

DEPARTMENT: Obstetrics and Gynecology  
SERVICE: Gynecologic Oncology Group

STATUS: N  
INITIAL APPROVAL DATE: 30 September 2003

### STUDY OBJECTIVE

To determine the frequency of histopathological markers (HPM) or precursor lesions of the ovaries, including surface papillomatosis, invaginations, pseudostratification, and inclusion cysts removed from participants in the two arms of the clinical trial (surgery and fenretinide treated).

To determine the relative avoidance of markers of cell proliferation and apoptosis in cancer-prone ovaries from fenretinide-treated patients of the clinical trial. This will permit the establishment of baseline values of these surrogate endpoint biomarkers (SEBs) in high-risk populations as well as to evaluate the specific impact of fenretinide treatment on cell proliferation and apoptosis in precursor lesions of an ovarian cancer-prone population.

### TECHNICAL APPROACH

This exploratory study will characterize ovarian tissue taken from women at high risk for ovarian cancer who have elected prophylactic oophorectomy and who have been randomized to receive either immediate surgery or Fenretinide pre-operatively.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Mutation of Analysis of Fumarate Hydratase in Sporadic Uterine Leiomyoma

KEYWORDS:

PRINCIPAL INVESTIGATOR: Maxwell, G. Larry, MAJ MC

ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 1 October 2002

### STUDY OBJECTIVE

To determine if the familial leiomyoma gene, fumarate hydratase, is altered in patients with sporadic leiomyoma.

To perform loss of heterozygosity analysis to determine if other regions in chromosome 1q are altered in patients with sporadic leiomyoma.

### TECHNICAL APPROACH

The study will be a descriptive pilot genetic study to determine if fumarate hydratase is altered in sporadic leiomyomas. Clinical data will not be assessed as part of this descriptive genetic study. Abnormalities in the genetic sequence will be correlated with both expression and functional status of the *FH* gene.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Procurement of Follicular Fluid For Studies of Granulosa Cell Function

KEYWORDS:

PRINCIPAL INVESTIGATOR: Neithardt, Adrienne B., 2LT MC

ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 5 November 2002

### STUDY OBJECTIVE

To determine whether factors in follicular fluid apart from the inhibin-activin family affect luteinizing hormone (LH) secretion.

### TECHNICAL APPROACH

We will first test for LH activity and then fractionate the follicular liquid by a variety of methods to determine the fraction in which the LH activity resides. Then we will use mass spectroscopy and Western gels to identify specific proteins and will perform mini-sequencing to identify partial amino acid structure. Substances within the follicular fluid will be assayed and correlated with the effects of gonadotrope secretion. Follicular fluid obtained during egg retrieval for *in vitro* fertilization at WRAMC will be used as the source of fluid and granulosa cells. This fluid would normally be discarded as biologic waste at the time of retrieval and the department of pathology never receives any specimens. We will split samples at WRAMC (using NIH supplies and dry ice) to evaluate if samples perform differently when transported in ice water versus initial freezing.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Bion® - An Implantable Microstimulator For The Chronic Treatment of Refractory Urinary Urge Incontinence

KEYWORDS:

PRINCIPAL INVESTIGATOR: Buller, Jerome L., MAJ MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 22 April 2003

### STUDY OBJECTIVE

To determine the efficacy of the bion® in the treatment of refractory urinary urge incontinence.  
To reduce by 50% the average number of leaks per day, as measured by the voiding diaries.  
To demonstrate an acceptable rate of adverse events.  
To evaluate the impact of bion® on the quality of life measures in patients with refractory urinary urge incontinence.  
To evaluate patient acceptance of chronic electrical stimulation of the pudendal nerve via the bion®.

### TECHNICAL APPROACH

This study is with an investigational device exemption (IDE) protocol evaluating chronic pudendal nerve stimulation using a miniature integrated stimulating electrode as an implantable micro-neurostimulator for the treatment of refractory urinary urge incontinence. This is a prospective randomized study designed to evaluate the use of the bion® for the treatment of urinary urge incontinence.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Digene Hybrid Capture® 2 – Validation of the Digene Rapid Capture System Using the Hybrid Capture® 2 HPV DNA Test

PRINCIPAL INVESTIGATOR: Elkas, John Christopher, LCDR, MC  
ASSOCIATES:

DEPARTMENT: Obstetrics and Gynecology  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 10 June 2003

### STUDY OBJECTIVE

To compare the performance of the manual version 2 HPV DNA Testing method to the HPV DNA investigational probe addition (PAO or manual-version-3) testing method when comparing results obtained from endocervical specimens collected with the broom collection device and rinsed into Cytec PreservCyt Solution or collected with Digene Cervical Sampler and STM (Specimen Transport Medium in the Digene Cervical Sampler). This will be an equivalency study, not a study to determine whether one method is better than the other.

To compare the performance of the semi-automated Rapid Capture System (RCS) Application for the HC2 HPV DNA Test to the HPV DNA-version-3 method when comparing results obtained from endocervical specimens collected with the broom collection device and rinsed into Cytec PreservCyt Solution or collected with Digene Cervical Sampler and STM (Specimen Transport Medium in the Digene Cervical Sampler). This will be an equivalency study, not a study to determine whether one method is better than the other.

### TECHNICAL APPROACH

WRAMC is a collection site only. We will be involved in the collection only and will ship the specimen to one of the designated testing sites for HC2 HPV Testing. Once testing is complete on the specimens, any portion remaining will be destroyed. Patients who are obviously pregnant or declare themselves pregnant will not be eligible for this study. No testing for pregnancy will be done. All patients will undergo their scheduled pap smear, which will be processed through the cytology laboratory at WRAMC in the normal fashion. After the scheduled pap smear is obtained, two additional cervical specimens will be collected from each woman who meets the study eligibility criteria and consents to participate in the study. All samples will be collected in the exact same manner. Approximately two micrograms of cells will be collected. The specimens will be collected according to the manufacturer's instructions. If an additional cervical specimen is required to be obtained for the clinic's diagnostic purposes, this specimen will be collected prior to the collection of the cervical specimen obtained for the study. The PreservCyt and STM specimens will be tested for HPV DNA following the Study Design Flow Chart for HC2 Testing and in accordance with the HC2 testing procedure. It is preferred, but not required, that specimens be tested by HC2 weekly, and no longer than two weeks after collection, following the specified specimen storage times and handling. Specimens will be stored at room temperature. In cases where PreservCyt specimens tested with the HPV Tests yield results around the cutoff (i.e.; with RLU/CO values between 0.8-5.0), repeat testing is required to enable final interpretation based on a retest algorithm utilizing all three test results. Results will be recorded on the Patient Case Report. Patients will not receive the results of testing done at Indiana University. Patients will only be informed of their Pap Smear results performed at WRAMC. If the patient decides to have the study specimens destroyed or identification removed from the specimen, they can do so by calling the principle investigator (if the specimen has not been processed).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: MRI Evaluation of the Contralateral Breast in Women With A Recent Diagnosis of Breast Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Choi, Jong-Ho R., MAJ MC

ASSOCIATES:

DEPARTMENT: Radiology

STATUS: N

SERVICE: Diagnostic Radiology

INITIAL APPROVAL DATE: 8 April 2003

### STUDY OBJECTIVE

This study involves having a magnetic resonance imaging (MRI) taken of the breast without cancer to determine if MRI is able to detect cancers that are not detectable by clinical breast exam or mammogram.

### TECHNICAL APPROACH

Up to 200 Military health care beneficiaries age 18 years and older presenting with the diagnosis of primary breast cancer will be asked to participate in this project at Walter Reed Army Medical Center. A total of 1000 patients will be enrolled in the overall multi-center clinical trial.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Hybrid Capture/In-Situ Hybridization (HCISH) Comparative Study For Human Papillomavirus Testing On Pap Test

KEYWORDS:

PRINCIPAL INVESTIGATOR: Kaplan, Keith J., MAJ MC  
ASSOCIATES:

DEPARTMENT: Pathology and Area Laboratories  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 26 November 2002

### STUDY OBJECTIVE

1. To compare the performance of two molecular assays used for HPV testing on Pap tests with results of "atypical squamous cells of undetermined significance" (ASCUS).
2. To document the sensitivity and specificity of each assay using the cervical biopsy as the gold standard, with in-situ HPV testing on cervical biopsy tissue.
3. To elucidate the advantages and disadvantages of each technique for directing clinical management of atypical pap smears.

### TECHNICAL APPROACH

The study is a prospective observational, double blind study. Researchers will be blinded to the results of the HPV testing until all of the data is compiled. There is no deviation from the current standard of care regarding appropriate patient triage and follow-up. All patients with an ASCUS result will receive HC II® testing for HPV DNA if they have adequate sample. Patient samples that are insufficient for testing by both methods will not be included in the study. The correlation results will not be tabulated or disclosed until the end of the study and health care providers and patients will not have access to this information.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: Implementation of the SARS Coronavirus Real-Time PCR Primers and Probes Assay

KEYWORDS:

PRINCIPAL INVESTIGATOR: Craft, David W., LTC MC

ASSOCIATES:

DEPARTMENT: Pathology and Area Laboratories

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 24 June 2003

### STUDY OBJECTIVE

To distribute SARS Coronavirus Real-time PCR Primers and Probes to participating LRN laboratories. Once available within the LRN, this device is to be used in real-time PCR assays to detect SARS Coronavirus RNA in respiratory specimens and as a surveillance tool allowing public health authorities to respond to the outbreak and limit transmission of this agent.

### TECHNICAL APPROACH

Health care providers will be instructed through web-based documents that SARS Coronavirus testing will be available for evaluation of SARS symptomatic patients and their close contacts. A minimum of the first 50 specimens sent to the LRN laboratories will be split with one aliquot sent to CDC for confirmatory testing along with a copy of the completed specimen submission form.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: CD 40 Expression in Thyroid Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Francis, Gary L., COL MC  
ASSOCIATES:

DEPARTMENT: Pediatrics  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 20 May 2003

### STUDY OBJECTIVE

1. To determine the presence or absence of insulin-like growth factor-1 (IGF-1) and IGF-2 expression in a group of benign and malignant thyroid tumors from children and adolescents.
2. To determine the presence or absence of type-1 IGF receptor (IGF-R1) and insulin receptor type A (IR-A) expression in a group of benign and malignant thyroid tumors from children and adolescents.
3. To compare the expression of IGF-1, IGF-2, IGF-R1, and IR-A between benign and malignant thyroid tumors.
4. To correlate the presence or absence of IGF-1, IGF-2, IGF-R1, and IR-A expression with the presence of metastasis or recurrence among the malignant thyroid tumors.

### TECHNICAL APPROACH

This is an observational study that will determine the presence of IGF-1, IGF-2, IGF-R1, and IR-A immunostaining in a group of benign and malignant thyroid lesions from children. The expression of each factor will be entered into the computerized database and correlated with the clinical outcomes listed above.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Randomized Placebo-Controlled Trial of Citalopram For Anxiety Disorders Following Traumatic Brain Injury

KEYWORDS:

PRINCIPAL INVESTIGATOR: Warden, Deborah L., M.D. DAC

ASSOCIATES: Kara S. Comins, B.S., LTC(P) James Ecklund, MC, Louis M. French, Psy.D., Maria E. Graves, RN, COL Robert J. Labutta, MC, Elisabeth Moy Martin, RNC, MA, Kim Mohres, B.S., Gwendolyn E. Roberson, M.A., Laurie M. Ryan, Ph.D., Karen Schwab, Ph.D., Molly B. Sparling, B.A.

DEPARTMENT: Neurology  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 10 December 2002

### STUDY OBJECTIVE

The proposal will assess the effectiveness of SRI treatment of generalized anxiety disorder due to TBI. We hypothesize that participants will report significantly fewer and less severe anxiety symptoms after a 12-week course of citalopram than after a 12-week course of placebo.

### TECHNICAL APPROACH

A randomized placebo controlled clinical trial design will be used to investigate the effectiveness of citalopram in patients with anxiety disorder due to a general medical condition, specifically traumatic brain injury (TBI). Beneficiaries who are between 6 and 14 months post injury and who meet criteria for DSM-IV diagnosis of anxiety disorder due to TBI will be recruited from the 7 DVBIC VA and Military Medical Centers. Participants will be randomized to receive an increasing dose of citalopram or placebo up to a dose of 40 mg of citalopram or 4 tablets of placebo over a 12-week treatment period. Patients will receive comprehensive multidisciplinary evaluations at a DVBIC site, including neurology, neuropsychology and psychiatry interviews and evaluations at baseline, 12 weeks and 12 months. Primary outcome measures will include the clinician rated DSM-IV anxiety disorder criteria and the patient report Spielberger State Anxiety Inventory.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Efficacy of Quetiapine in Migraine Prophylaxis and Quantification of Migrainous Symptoms Via Actigraphy

KEYWORDS:

PRINCIPAL INVESTIGATOR: Labutta, Robert, COL MC  
ASSOCIATES:

DEPARTMENT: Neurology  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 14 January 2003

### STUDY OBJECTIVE

It is hypothesized that patients who receive Quetiapine, a novel dibenzothiazapine, can experience a significant reduction in the frequency of migraine attacks and/or the average severity of attacks. We intend to evaluate the efficacy of quetiapine in the prevention of migraine via a preliminary double-blind study with a placebo-controlled design. The protocol is aimed at defining specific actigraphic signal characteristics of migraine and discerning whether actigraphy can be used to evaluate therapeutic responses.

### TECHNICAL APPROACH

The study will be conducted using the drug Seroquel™, which has been approved by the FDA for the treatment of schizophrenia, but has not been approved for use with migraine headache. The current standard of care for migraine involves various abortive treatment regimens to alleviate migrainous attacks. However, due to the variability of effectiveness of abortive medications for migraine, this study attempts to investigate the efficacy of an atypical neuroleptic as a preventive measure for the management of migraine. This study is a prospective, randomized, double blind, placebo-controlled trial comparing the efficacy of Quetiapine versus placebo in migraine headache prevention. The present study is stratified into two separate phases, a dose-finding pilot phase, and an efficacy phase.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Protocol No CENA713BUS11 – A 12-Week, Prospective, Double-Blind, Placebo-Controlled, Multi-Center Study Evaluating the Efficacy and Safety of Exelon® 3 to 6mg/day in Patients With Traumatic Brain Injury (TBI) With Persistent Cognitive Deficits

### KEYWORDS:

PRINCIPAL INVESTIGATOR: Warden, Deborah L., M.D. DAC

ASSOCIATES: Kara S. Comins BS, Kim Mohres, BS, Elizabeth Moy Martin, RNC, MA

DEPARTMENT: Neurology

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 25 February 2003

### STUDY OBJECTIVE

#### Primary:

- Efficacy: to examine the efficacy of open-label Exelon® in patients with traumatic brain injury with persistent cognitive impairments on improvement in cognitive functioning in the areas of attention or verbal memory.
- Safety: to assess the safety and tolerability of Exelon® in patients with traumatic brain injury with persistent cognitive impairment.

#### Secondary:

- To examine the effects of Exelon® on cognitive functioning in the areas of verbal memory and recall, attention, divided attention, information processing, processing speed, spatial working memory, executive functioning, verbal fluency, and word finding ability.
- To examine the effects of Exelon® on behavior, depression, and quality of life.
- To examine the effects of Exelon® on change in overall functioning.
- To provide continued treatment of Exelon® to patients with traumatic brain injury with persistent cognitive deficits.

### TECHNICAL APPROACH

Patients will be male or female, aged 18-50 years of age, and living in the community. Completion of the double-blind phase of the study is required for eligibility for the open-label extension of this study. All patients who successfully complete the double-blind treatment period will be invited to participate in this extension. Therefore, up to 15 patients from WRAMC who participated in Protocol CENA713BUS1 1 will participate in this open-label extension study.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Post-Text Supplement 1 – 26-Week Open-Label Extension to Protocol No. CENA713BUS11 – A 12-Week, Prospective, Double-Blind, Placebo-Controlled, Multi-Center Study Evaluating the Efficacy and Safety of Exelon® 3 to 6mg/day in Patients With Traumatic Brain Injury (TBI) With Persistent Cognitive Deficits

KEYWORDS:

PRINCIPAL INVESTIGATOR: Warden, Deborah L., M.D. DAC

ASSOCIATES:

DEPARTMENT: Neurology

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 25 February 2003

### STUDY OBJECTIVE

Please refer to page 6, section 2 of sponsor Post-text Supplement 1.

### TECHNICAL APPROACH

The drug to be used in this study, Exelon® (rivastigmine tartrate), was approved by the United States Food and Drug Administration (FDA) in April 2000 for the treatment of mild to moderate dementia of Alzheimer's type. Exelon® will be used in this study under IND# 35774 (date of submission 7 November 1990 by Novartis Pharmaceutical Corporation) to evaluate its safety and effectiveness in the treatment of persistent cognitive deficits resulting from a traumatic brain injury. A copy of the Investigator's Brochure is on file in the Research Review Service, Department of Clinical Investigation.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Neurological Apathy as a Model For Schizophrenia With Primary Negative Symptoms

KEYWORDS:

PRINCIPAL INVESTIGATOR: Warden, Deborah L., M.D. DAC

ASSOCIATES:

DEPARTMENT: Neurology

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 11 March 2003

### STUDY OBJECTIVE

A research protocol being conducted by investigators at Johns Hopkins University is investigating the similarities between the negative features of schizophrenia with apathy symptoms experienced after brain injury in an attempt to elucidate the underlying pathophysiology. The specific aim of the research protocol at Johns Hopkins is to elucidate the clinical and pathological features of patients with schizophrenia with deficit syndrome in comparison with traumatic brain injury patients with apathy by clinical measures and structural neuroimaging methods. The Defense and Veterans Brain Injury Center (DVBIC) at Walter Reed Army Medical Center will participate by screening patients for inclusion as subjects in this Johns Hopkins University research protocol.

### TECHNICAL APPROACH

WRAMC investigators will screen traumatic brain injury patients with the Apathy Evaluation Scale and a form outlining the other criteria for participation to determine whether they meet the entry criteria for the study. Subjects who meet entry criteria (score of > 30 on the scale, matches inclusion criteria, has no exclusion criteria) will be invited to go to Johns Hopkins University for a formal assessment.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Conduction Time For a 6-Centimeter Segment of Ulnar Nerve Across The Elbow – Reference Values

KEYWORDS:

PRINCIPAL INVESTIGATOR: Landau, Mark E., LTC MC  
ASSOCIATES:

DEPARTMENT: Neurology  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 8 April 2003

### STUDY OBJECTIVE

The ultimate goal is to develop a new electrodiagnostic technique for diagnosing Ulnar Nerve Mononeuropathy at the elbow (UNE). This is a preliminary study to attain reference values for conduction times of the motor component of the ulnar nerve across the elbow.

### TECHNICAL APPROACH

This is an open-label, observational study. A focused history and neurological examination of the upper extremities will be performed. Patients will be asked about any pain, numbness, paresthesia, or weakness of the arms. The arms will be inspected for atrophy. The strength, sensation and reflexes of the arms will also be performed. Only patients with a normal assessment will continue.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: Detection of Spreading Depression in Stroke Using Non-Invasive Electroencephalography

KEYWORDS:

PRINCIPAL INVESTIGATOR: Landau, Mark E., LTC MC

ASSOCIATES:

DEPARTMENT: Neurology

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 13 May 2003

### STUDY OBJECTIVE

This pilot study seeks to determine whether spreading depression (SD), a cerebral electrical event recorded in animals with stroke, can be detected in human stroke patients via scalp electroencephalographic (EEG) recordings.

### TECHNICAL APPROACH

This is an observational study with the intent to determine whether the phenomenon of cortical SD can be documented via scalp EEG recordings in human stroke patients. The scientific hypothesis is that SD is an inherent sequela of ischemic injury in humans. This assumption has not been demonstrated previously for patients with thrombotic/embolic stroke. The methodological hypothesis is that the signature electrical silence of SD, occurring in the context of ischemia, can be detected via a closely spaced array of scalp EEG recording electrodes.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Novel Calcium Pool in Rat CNS

KEYWORDS:

PRINCIPAL INVESTIGATOR: Watson, William D., LCDR MC  
ASSOCIATES:

DEPARTMENT: Neurology  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 5 August 2003

### STUDY OBJECTIVE

To determine whether or not the TG-I  $\text{Ca}^{2+}$  uptake we have previously described is actually the activity of the secretory pathway calcium ATPase (SPCA).

### TECHNICAL APPROACH

Animals will be euthanized by  $\text{CO}_2$  and their brains carefully removed and regionally dissected to produce samples of forebrain, cerebellum, and brain stem. Sub-cellular fractions of microsomes will be prepared by differential centrifugation as published (Verma, Hirsch, et al 1990). Accumulation of calcium into microsomes by  $\text{Ca}^{2+}$ -ATPase activity will be monitored by incubating at  $37^\circ\text{C}$  in a HEPES buffer (pH 7.3) containing polyethylene glycol, sodium azide, DTT,  $\text{MgCl}_2$ , ATP,  $\text{CaCl}_2$ , and  $^{45}\text{Ca}^{2+}$  or  $^{54}\text{Mn}^{2+}$  as a radiolabelled tracer. Reactions will be performed in 96-well glass fiber filter Millipore plates with each experiment standardized for protein content. Experiments will be terminated by rapid filtration via a Millipore plate vacuum and the filters washed twice with ice-cold wash buffer. Retained radioactivity indicating  $^{45}\text{Ca}^{2+}$  or  $^{54}\text{Mn}^{2+}$  accumulation into sub-cellular compartments will be determined by liquid scintillation counting. Using similar uptake and wash buffers,  $^{45}\text{Ca}^{2+}$  or  $^{54}\text{Mn}^{2+}$  accumulation can also be visualized by autoradiography in permeabilized fresh frozen brain tissue sections (Verma, Hirsch, et al 1992).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Defense and Veterans Brain Injury Center (DVBIC) WRAMC Core Evaluation Protocol

KEYWORDS:

PRINCIPAL INVESTIGATOR: Warden, Deborah L., MD DAC

ASSOCIATES: Kara Comins, BS, LTC(P) James Ecklund, MC, Louis French, Psy.D., Kelly Gourdin, BS, Maria E. Graves, RN, COL Robert Labutta, MC, Elisabeth Moy Martin, RNC, MA, Thomas Maryniak, BA, Kim Mohres, BS, Gwendolyn E. Roberson, MA, Laurie M. Ryan, Ph.D., Karen Schwab, Ph.D., Jose Valls, BS, Molly B. Sparling, BA

DEPARTMENT: Neurology  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 26 August 2003

### STUDY OBJECTIVE

Overall objectives of the Defense and Veterans Brain Injury Center (DVBIC): To ensure that all military and VA traumatic brain injured (TBI) patients receive TBI-specific evaluation and follow-up, while at the same time collecting standardized patient outcome data that will allow us to evaluate the relative efficacy and cost of various TBI treatment and rehabilitation strategies, and to define optimal care for victims of TBI.

Specific objectives: Our initial protocol completed at WRAMC (WU #7144) with the collaboration of the national DVBIC has contributed to the establishment of a standardized TBI registry and tracking system, a network of collaborative TBI centers of excellence at major military hospitals, and a comprehensive TBI evaluation that has become the standard of care for TBI patients at WRAMC. A recent publication in JAMA as a result of this research provides evidence guiding rehabilitation strategies in TBI (Salazar, et al, 2000). Although clearly much has been learned from our previous studies, there is still more knowledge to be gained through the ongoing study of patients referred for comprehensive evaluation in the TBI program at WRAMC. Therefore this protocol requests permission to analyze the collected data in a descriptive, observational study. In order to better understand the impact of traumatic brain injury on functioning, up to 50 healthy controls will be recruited to participate in a shortened evaluation battery.

### TECHNICAL APPROACH

This is a prospective, descriptive, observational study. Data on up to 500 TBI patients collected within the current standard of care evaluations at WRAMC will be analyzed. In order to better understand the impact of traumatic brain injury on functioning, up to 50 healthy controls will be recruited to participate in a shortened evaluation battery.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Prevalence Study of Chronic Problems and Sequelae After Traumatic Brain Injury in the Military and Veteran Populations

KEYWORDS:

PRINCIPAL INVESTIGATOR: Schwab, Karen A., Ph.D. DOD

ASSOCIATES: Deborah L. Warden, MD, Kelly Gourdin, BS, Laurie M. Ryan, Ph.D., Manjula Ramareddy, Ph.D., Brian Ivins, MPS

DEPARTMENT: Neurology  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 26 August 2003

### STUDY OBJECTIVE

This study will investigate the extent and severity of chronic sequelae and poor outcomes after TBI in active duty and retired military populations. Reliable information on chronic sequelae of TBI is not available for civilian or military populations. The goal of the study is to provide evidence on the consequences of TBI to health care researchers and military policy makers in order that future studies and treatment programs can be developed to improve the care provided active duty and recently discharged and retired military populations with TBI. The findings will immediately inform clinicians whether or not TBI patients require routine follow-up.

### TECHNICAL APPROACH

This is a descriptive, observational study comparing symptoms and problems associated with TBI for former military and DVA patients known to have had TBI and registered in the DVBIC Head Injury Registry and uninjured friend/relative controls nominated by consenting subjects. A follow-up questionnaire based upon the Centers for Disease Control and Prevention (CDC) prevalence study in South Carolina will be used for the documentation of TBI sequelae. The use of a set of common questions will permit an eventual comparison of findings from the two studies.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Establishing a Military Nursing Outcomes Database

KEYWORDS:

PRINCIPAL INVESTIGATOR: Patrician, Patricia A., LTC AN  
ASSOCIATES:

DEPARTMENT: Nursing  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 3 December 2002

### STUDY OBJECTIVE

The global aim of this long term, multi-staged military nursing research program is to create and implement a high quality database consisting of data related to nurse staffing effectiveness and patient safety indicators. This current proposal represents Stage Three of the nursing relevant database research program. The aim of this stage is to expand and sustain a high quality military patients safety and nurse staffing effectiveness database. This will be accomplished by increasing the scope and impact of the Army Nursing Outcomes Database (ANOD) developed in Stage Two and transforming it into the Military Nursing Outcomes Database (MilNOD).

### TECHNICAL APPROACH

Data will be collected from both primary and secondary sources. Primary sources of data will include the established nursing care structural indicators, patient outcome indicators, and a nursing outcome indicator. In addition, a goal is to develop mechanisms for collecting data for two new indicators – “nurse committed medication errors” and “nursing staff needle stick injuries”, and two new explanatory variables – “patient turnover” and “patient acuity”. This is a multi-site, clinical study with multiple repeated and point-in-time measures. The research design is both observational and descriptive.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Patient Handling Interventions at a Major Military Medical Facility

KEYWORDS:

PRINCIPAL INVESTIGATOR: Patrician, Patricia A., LTC MC

ASSOCIATES:

DEPARTMENT: Nursing

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 17 June 2003

### STUDY OBJECTIVE

Objective 1. To compare the effect of patient handling demands by level of patient dependencies and transfer types that occur during a 24-hour period on five inpatient units before and after intervention.

Objective 2. To decrease the physiological effect of transfers in terms of discomfort level and physical exertion based on patient dependency level, type of transfer, and type of shift as compared to pre-intervention baseline discomfort and exertion.

Objective 3. To evaluate various forms of intervention based on user feedback and surveys. These interventions will include command emphasis, equipment implementation and training, an awareness campaign, training for nursing staff and nursing head nurses, and system support. These components will be considered individually for analysis.

Objective 4. To describe the effects of the intervention six months after implementation. The effects of intervention will be described based on survey responses. These surveys will be compared with the baseline survey information. Additional walk-through observation surveys will be used to assess the head nurse's perceptions and staff compliance throughout the investigation.

### TECHNICAL APPROACH

This intervention study seeks to evaluate appropriate intervention based on the factors found to be associated with patient handling discomfort on inpatient units at WRAMC and to describe the effects of the intervention.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Army Women's Information Needs for Sexual Health Promotion

KEYWORDS:

PRINCIPAL INVESTIGATOR: LTC Elmer Wayne Combs, Ph.D., AN  
ASSOCIATES:

DEPARTMENT: Nursing  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 22 July 2003

### STUDY OBJECTIVE

Specific Aim: Conduct a large-scale survey of Army women to answer the following research questions: What types of information about pregnancy and sexually transmitted infections (STI) prevention have they received before? What was useful and not useful about past information? How did this past information influence their sexual behavior? What types of information and products would they like to receive for deployment situations? What is the level of sexual risk behavior among military women? What are their perceptions about condom use? Are Army women who respond to the survey representative of the demographic characteristics of women in that service?

### TECHNICAL APPROACH

The rates of sexually transmitted infections and unintended pregnancies among the general population and military women continue to be of concern. Although sexual activity among service members is prohibited during deployment, the conditions of deployment may cause men and women to turn to each other for sexual gratification, and assurance of safety, love, and belonging - the most fundamental of human needs (Maslow, 1970). The result of sexual activity can be an STI or an unintended pregnancy. The unique needs of deployed military women must be met by research- and theory-based strategies. However, the primary step in developing such a strategy is to determine what types of information women need for sexual health promotion/reduction of risky sexual behavior. The purpose of the proposed study is to determine those needs.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: An Exploratory Study of the Psychosocial Effects of Stress Urinary Incontinence and Coping Strategies Among Military Women

KEYWORDS:

PRINCIPAL INVESTIGATOR: Criner, Judy A., MAJ AN  
ASSOCIATES:

DEPARTMENT: Landstuhl Regional Medical Center  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 18 March 2003

### STUDY OBJECTIVE

To describe to symptom distress associated with Stress Urinary Incontinence (SUI) in military women. To investigate how barriers to continence affect coping and quality of life in military women with SUI while in the field environment.

### TECHNICAL APPROACH

The PI will conduct exploratory research using one large sample from different locations in Germany. The major variables of interest are symptom distress, self-esteem, coping, and quality of life, and the relationships thereof.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: Perceptions of Splint Wear Between Two Splints For a Person With Hand Injury

KEYWORDS:

PRINCIPAL INVESTIGATOR: Ms. Susan A. Gray, Civilian

ASSOCIATES: MAJ Steven Gerardi MC

DEPARTMENT: Landstuhl Regional Medical Center

SERVICE:

STATUS: N

INITIAL APPROVAL DATE: 5 June 2003

### STUDY OBJECTIVE

This study is a pilot designed to collect baseline descriptive data from one patient concerning the level of satisfaction, function, and comfort of two different types of hand splints. Additionally, this study will test a questionnaire designed by the PI specifically for this study. The objective of this study is to be able to determine the level of satisfaction, function, and comfort between a radial-based resting hand splint and a volar-based resting hand splint. Also, problems will be identified so that a larger prospective study comparing two groups at a later date may be performed.

### TECHNICAL APPROACH

Up to one subject, military health care beneficiaries age 18 years and older presenting with the diagnosis of hand injury that would be indicated for wearing a resting hand splint including DeQuervain's and carpal tunnel syndrome.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Epidemiology and Analysis of Syphilis in a Long-Term Military Cohort of Human Immunodeficiency Virus-Infected Individuals

KEYWORDS:

PRINCIPAL INVESTIGATOR: Katherine Spooner, MD, CIV, DOD

ASSOCIATES: Glenn Wortmann, LTC, MC, Clifton Hawkes, LTC, MC

DEPARTMENT: Medicine

STATUS: N

SERVICE: Infectious Disease

INITIAL APPROVAL DATE: 9 September 2003

### STUDY OBJECTIVE

Define the epidemiology of syphilis in a cohort of HIV-infected individuals in patients who have been followed in the Natural History Study. The time period for evaluation includes July of 1987 when the protocol was initiated until submission of this retrospective protocol in August of 2003. We will specifically look at patients enrolled in the Natural History Study of HIV infection and include those that have a diagnosis of syphilis entered into the database. In these patients with both HIV infection and syphilis, we will evaluate demographics, level of immunocompromised from HIV, presence or history of other sexually transmitted diseases, and how many episodes of syphilis were diagnosed in each patient.

Evaluate the treatment and response to treatment of syphilis in the presence of HAART versus the absence of HAART.

### TECHNICAL APPROACH

A retrospective analysis of syphilis data in a military cohort is planned. These patients previously enrolled in a multi-site U.S. Military Natural History Study of HIV and AIDS, and patients will be identified by a diagnosis of syphilis in the database. Data will be extracted from the existing database and confirmed through source documents.

Data to be collected and evaluated includes: incidence of false positives, rates per person/year, demographics (age, race, sex), rates of second/third episode, rate of response to treatment in presence of HAART vs. no HAART, CD4/viral load and relation to RPR titer, numbers of prior/concomitant sexually transmitted diseases, incidence of neurosyphilis, and documentation of assays used in diagnosis.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Management of Anemia and Neutropenia Associated With Pegylated Interferon + Ribavirin  
Treatment of Chronic Hepatitis C – An Open-Label Dose Titration Study of Darbepoetin Alfa and  
Filgrastim

KEYWORDS:

PRINCIPAL INVESTIGATOR: Sjogren, Maria H., COL MC  
ASSOCIATES:

DEPARTMENT: Clinical Investigation  
SERVICE:

STATUS: N  
INITIAL APPROVAL DATE: 11 February 2003

### STUDY OBJECTIVE

The primary objective of this study is to evaluate the potential role of Darbepoetin alfa and Filgrastim in preventing two important side effects of this combination therapy allowing for the delivery of higher doses of ribavirin and PEG interferon alpha-2b. It is hypothesized that by preventing ribavirin-induced anemia, the side effect profile will improve, enhancing both HRQL and the efficacy of this antiviral regimen as evidenced by viral eradication in these patients. The secondary objective of this study is to identify the dose of Darbepoetin alfa required to maintain an average increase in hemoglobin of >2g/dL and the dose of Filgrastim required to maintain an average absolute neutrophil count above  $1.5 \times 10^9/\text{L}$  for the management of combination HCV therapy-induced cytopenia.

### TECHNICAL APPROACH

This study is an open-label pilot dose titration study. Up to twenty-five patients are expected to enroll in this study from WRAMC. Patients will be eligible to participate in this study if all inclusion and no exclusion criteria apply. All subjects will be required to sign an informed consent form before participating.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: A Functional Co-Culture of Hepatocytes and Hepatic Stellate Cells

KEYWORDS:

PRINCIPAL INVESTIGATOR: Rojkind, Marcos, Dr.

ASSOCIATES:

DEPARTMENT: Clinical Investigation

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 5 August 2003

### STUDY OBJECTIVE

The main goal of this proposal is to develop long-term cultures of hepatocytes suitable for reproducing physiological and pathological events occurring *in vivo* in the intact liver.

### TECHNICAL APPROACH

We propose to establish co-cultures of hepatocytes with hepatic stellate cells (HSC), the main extracellular matrix producing cells of the liver, and thus replicate in culture part of the liver microenvironment.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Evaluation of Dendritic Cell Functions During Hepatitis C Virus Infection and IFNa/Ribavirin Therapy

KEYWORDS:

PRINCIPAL INVESTIGATOR: Zhou, Yaling, Ph.D. DAC

ASSOCIATES: COL Maria H. Sjogren, MC, Yvonne Lukes, Brian Reinhardt

DEPARTMENT: Clinical Investigation

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 23 September 2003

### STUDY OBJECTIVE

1. To determine the effect of HCV infection and IFNa/Ribavirin therapy on the biology of dendritic cells including their phenotype, maturation, and functions.
2. To explore the correlation of the dendritic cell function with the responsiveness of HCV patients to IFNa/Ribavirin therapy.

### TECHNICAL APPROACH

This study is aimed to evaluate the phenotype and functions of dendritic cells during HCV infection and to explore the correlation of the dendritic cell function with the responses of patients to IFNa (interferon-alpha)/Ribavirin therapy. We plan to determine the effect of HCV infection and IFNa/Ribavirin therapy on the phenotypic change of dendritic cells by flow cytometry (FACS) analysis of their expression levels of several important surface molecules including CD1a, CD11c, CD54, CD80, CD83, CD86, and MHC class II (HLA-DR). We will also conduct ELISA assays to determine the levels of cytokines IL-12 and IL-10 produced by patients' dendritic cells before and after IFNa/Ribavirin treatment. In addition, we will determine the capacity of HCV-DC to stimulate T cell proliferation or cytokine (IFNg) production in a mixed leukocyte reaction (MLR). Finally, we will assess the effect of HCV infection and IFNa/Ribavirin therapy on the maturation of dendritic cell. These assays will be performed at selected time points (at weeks 0, 12, 24, 36, 48, 60, and 72) spanning the entire course of the IFNa/Ribavirin therapy as well as the post-therapy follow-up period. We will correlate the results from the DC functional study to the clinical responsiveness of patients to the IFNa/Ribavirin therapy. The results from this study will provide us with useful information on how dendritic cells function during the course of HCV infection, during antiviral therapy, and after the therapy. The information obtained will help us better understand the immune responses during HCV infection and during antiviral therapy with IFNa/Ribavirin. It will also help us plan for the next phase of the study to investigate the function of T cells during the HCV infection and antiviral therapy.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Changes in Nutritional Status of Hospitalized Patients – Implications Toward Clinical Outcomes

KEYWORDS:

PRINCIPAL INVESTIGATOR: Mobley, Stacey Lloyd, 2LT SP

ASSOCIATES:

DEPARTMENT: Nutrition Care Directorate

STATUS: N

SERVICE:

INITIAL APPROVAL DATE: 1 April 2003

### STUDY OBJECTIVE

To assess changes in nutritional status of hospitalized patients by evaluating nutritional screening forms, anthropometry, and handgrip dynamometry, and relate those changes to clinical outcomes. The specific aims include:

1. Establishing the prevalence of malnutrition in a large, military hospital setting.
2. Comparing and validating current nutritional screening and assessment tools.
3. Characterizing the changes of nutrition status during the course of hospital stay.
4. Identifying nutrition-related factors that are associated with clinical outcomes.

### TECHNICAL APPROACH

All hospitalized patients from General Medicine, General Surgery, and Oncology will be studied. The recruitment goal is 120 patients. Patients will be recruited within 72 hours of hospital admission. Dietetic interns from the U.S. Military Dietetic Internship Consortium at WRAMC will assess the patients' nutritional status. The patients' medical records will also be reviewed to determine the presence of complications during hospitalization.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

## DETAIL SUMMARY SHEET

TITLE: Diagnostic Accuracy of Shoulder Exam Tests

KEYWORDS:

PRINCIPAL INVESTIGATOR: Walsworth, Matthew, CPT SP  
ASSOCIATES:

DEPARTMENT: Orthopaedics and Rehabilitation

STATUS: N

SERVICE: Physical Medicine & Rehabilitation

INITIAL APPROVAL DATE: 5 November 2002

### STUDY OBJECTIVE

1. Determine the diagnostic accuracy characteristics (sensitivity and predictive values) of individual shoulder examination clinical tests.
2. Determine the most predictive cluster of tests or patient history data for shoulder diagnoses.
3. Determine the inter-rater reliability of shoulder examination tests.
4. Determine the utility of the tests among three different clinical specialties – orthopaedic surgery, internal medicine, and physical therapy.

### TECHNICAL APPROACH

Subjects must have been selected for and agreed to shoulder surgery by the WRAMC orthopedics staff. After agreeing to participate, the patient's history will be reviewed and the patient will undergo three additional clinical exams by another orthopedic surgeon, internal medicine physician, and physical therapist. The clinicians performing the exam will be blinded to the results of the diagnoses and testing procedures previously performed by the examining surgeon and to the results of the other examiners. These results will not be presented to the treating surgeon unless it is felt that the patient may have a diagnosis that is not actually a glenohumeral joint problem. The operating surgeon will take arthroscopic photographs of the abnormal and normal tissue sites in the shoulder. These photos will be used by surgeon on research team to establish a diagnosis. Thus, the inter-rater reliability of the gold standard will be tested as well. If there is a contradiction between the two surgeons, the operative surgeon's diagnosis will be used as the gold standard for our data analysis.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS

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## DETAIL SUMMARY SHEET

TITLE: Functional Outcomes and Weight-Bearing Following Total Knee Reconstruction – Relationship to Quality of Life

KEYWORDS:

PRINCIPAL INVESTIGATOR: Springer, Barbara A., LTC SP  
ASSOCIATES:

DEPARTMENT: Orthopaedics and Rehabilitation  
SERVICE: Physical Medicine & Rehabilitation

STATUS: N  
INITIAL APPROVAL DATE: 11 March 2003

### STUDY OBJECTIVE

The primary objective is to investigate changes in functional outcomes, weight bearing (WB), and quality of life (QOL) pre and post implantation of total knee prostheses in comparison with normal control participants of comparable age and gender. Secondary objectives are to study the relationship between these functional tests and health-related QOL and to further validate the tests as functional measures through the addition of a commonly used functional outcome measure (Timed Up and Go Test).

### TECHNICAL APPROACH

The study design is a controlled prospective repeated measures trial. Participants selected for TKR surgery and age/gender-matched controls will be invited to participate in the study. After consenting in writing, each participant will complete the following five dependent variables: 1) SF-36, 2) WOMAC, 3) the Timed Up and Go, 4) Weight Bearing Squat, and the 5) Step Up/Over a 4 inch and an 8 inch block. These variables will be repeated three times for the TKR group: 6 weeks, 4 months, and 12 months post-intervention, and one time (QOL questionnaires only) for the control group at 12 months post intervention. These 12-month questionnaires for the control group participants will be conducted over the telephone by the principal or associate investigator, or a designated staff member. The independent variables will be Group (TKR vs. Controls) and Time (pre-operative, 6 weeks, 4 months, and 12 months post-operative).

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New protocol for FY03.

### CONCLUSIONS



## DETAIL SUMMARY SHEET

TITLE: The Effects of a Thoracolumbosacral Orthosis on Gait of Normal Subjects

KEYWORDS:

PRINCIPAL INVESTIGATOR: LTC Paul Pasquina MC, USA

ASSOCIATES: CDR Ross Moquin MC, USN, Jill L. Schuyler, MS, Barri L. Miller, MPT

DEPARTMENT: Orthopaedics and Rehabilitation

STATUS: N

SERVICE: Physical Medicine & Rehabilitation

INITIAL APPROVAL DATE: 9 September 2003

### STUDY OBJECTIVE

The objective of this study is to quantify the effect of a thoracolumbosacral orthosis (TLSO) on parameters of normal gait: temporal/spatial, kinematics, and kinetics.

### TECHNICAL APPROACH

The study design will be an experimental prospective study of up to 26 normal subjects. All subjects will walk with no orthosis and two bracing conditions. The no orthosis condition will act as each subject's own control. Standard gait parameters will be quantified while walking at a normal pace. The gait parameters examined include temporal and spatial data as well as kinematic and kinetic data. Kinematic and kinetic graphs will be generated. Information from all body joints at heel strike, toe off, stance, and swing will be evaluated for differences due to bracing.

### PRIOR AND CURRENT PROGRESS and REVIEW OF RECENT LITERATURE

New Protocol for FY03.

### CONCLUSIONS